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September 21–23, 1990, Hyatt Regency Chicago, Chicago, Illinois (Page 168)

Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons
February 18–20, 1991, San Francisco Moscone Center, San Francisco, California
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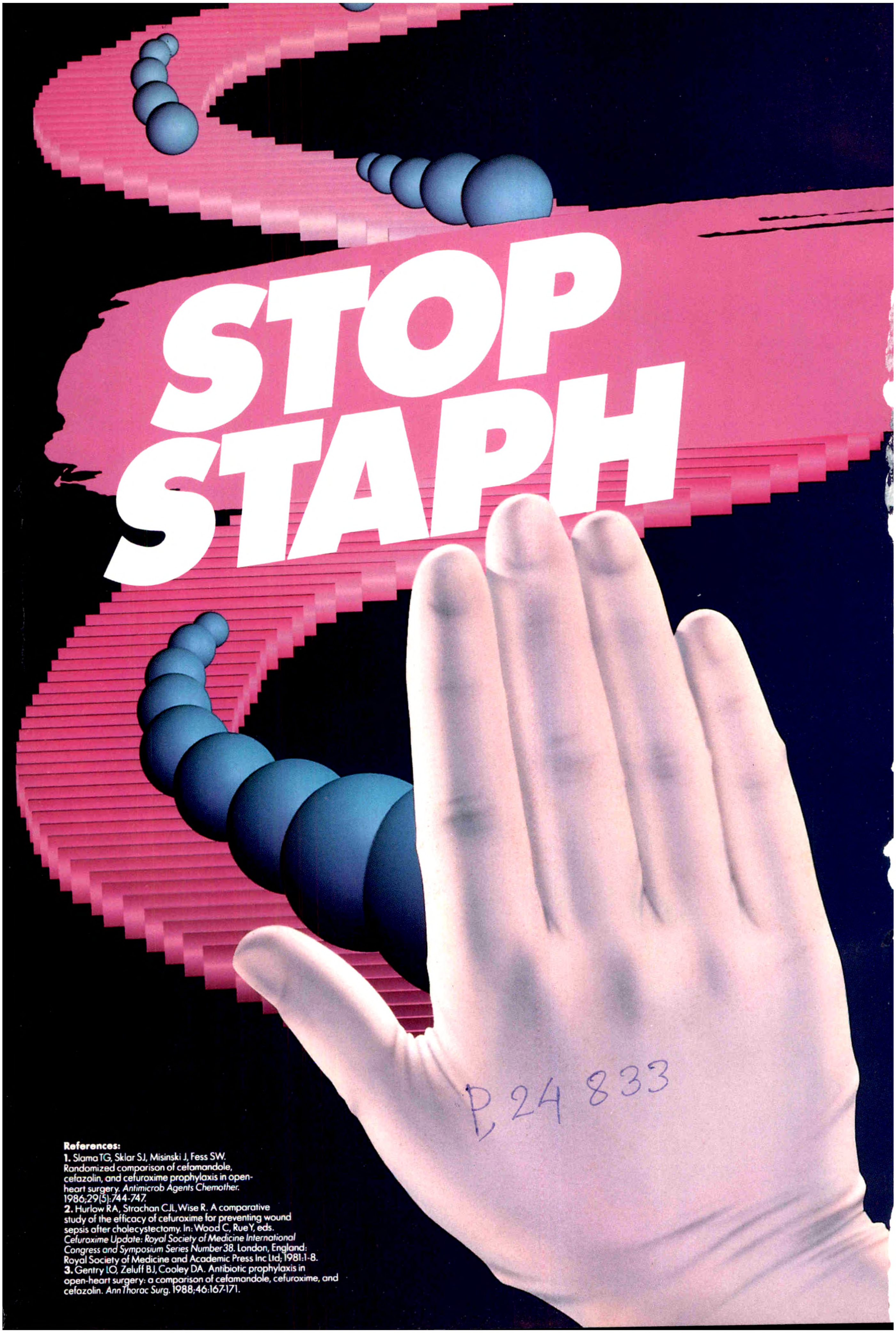

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For a complete listing of indications and usage, please consult Brief Summary of Prescribing Information for ZINACEF on adjacent page.

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Zinacef* (sterile cefuroxime sodium, Glaxo) **Zinacef*** (cefuroxime sodium injection) **BRIEF SUMMARY**

The following is a brief summary only. Before prescribing, see complete prescribing information in Zinacef* product labeling.

INDICATIONS AND USAGE: Zinacef* is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Lower Respiratory Tract Infections,** including pneumonia, caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), *Haemophilus influenzae* (including ampicillin-resistant strains), *Klebsiella* spp, *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pyogenes*, and *Escherichia coli*.
2. **Urinary Tract Infections** caused by *E coli* and *Klebsiella* spp.
3. **Skin and Skin Structure Infections** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, *E coli*, *Klebsiella* spp, and *Enterobacter* spp.
4. **Septicemia** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pneumoniae*, *E coli*, *H influenzae* (including ampicillin-resistant strains), and *Klebsiella* spp.
5. **Meningitis** caused by *S pneumoniae*, *H influenzae* (including ampicillin-resistant strains), *Neisseria meningitidis*, and *S aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea:** Uncomplicated and disseminated gonococcal infections due to *Neisseria gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *S aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. Zinacef has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to Zinacef.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, Zinacef may be used concomitantly with an aminoglycoside (see PRECAUTIONS). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The preoperative prophylactic administration of Zinacef may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (eg, vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. Zinacef should usually be given one-half to one hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of Zinacef has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that Zinacef therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: Zinacef* is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF* IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although Zinacef* rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Zinacef should be reduced in patients with transient or persistent renal insufficiency (see DOSAGE AND ADMINISTRATION), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Zinacef may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest® tablets), but not with enzyme-based tests for glycosuria (eg, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Zinacef.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since Zinacef is excreted in human milk, caution should be exercised when Zinacef is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: Zinacef* is generally well tolerated. The most common adverse effects have been local reactions following intravenous administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with intravenous administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in less than 1% of the patients treated with Zinacef and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in less than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (less than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence were seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Toxic epidermal necrolysis, fever, vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see DOSAGE AND ADMINISTRATION). If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Prolonged prothrombin time, pancytopenia, agranulocytosis, thrombocytopenia.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zinacef* product labeling.)

Impaired Renal Function: A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 1 in product package insert).

HOW SUPPLIED: Zinacef* in the dry state should be stored between 15° and 30°C (59° and 86°F) and protected from light. Zinacef is a dry, white to off-white powder supplied in vials and infusion packs as follows:

NDC 0173-0352-31	750-mg* Vial (Tray of 25)
NDC 0173-0354-35	1.5-g* Vial (Tray of 25)
NDC 0173-0353-32	750-mg* Infusion Pack (Tray of 10)
NDC 0173-0356-32	1.5-g* Infusion Pack (Tray of 10)
NDC 0173-0400-00	7.5-g* Pharmacy Bulk Package (Tray of 6)

Zinacef frozen as a premixed solution of cefuroxime sodium should not be stored above −20°C. Zinacef is supplied frozen in 50-ml, single-dose, plastic containers as follows:

NDC 0173-0424-00 750-mg* Plastic Container (Carton of 24)
NDC 0173-0425-00 1.5-g* Plastic Container (Carton of 24)

*Equivalent to cefuroxime.

October 1989
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Zinacef* (sterile cefuroxime sodium): Glaxo Pharmaceuticals, Research Triangle Park, NC 27709
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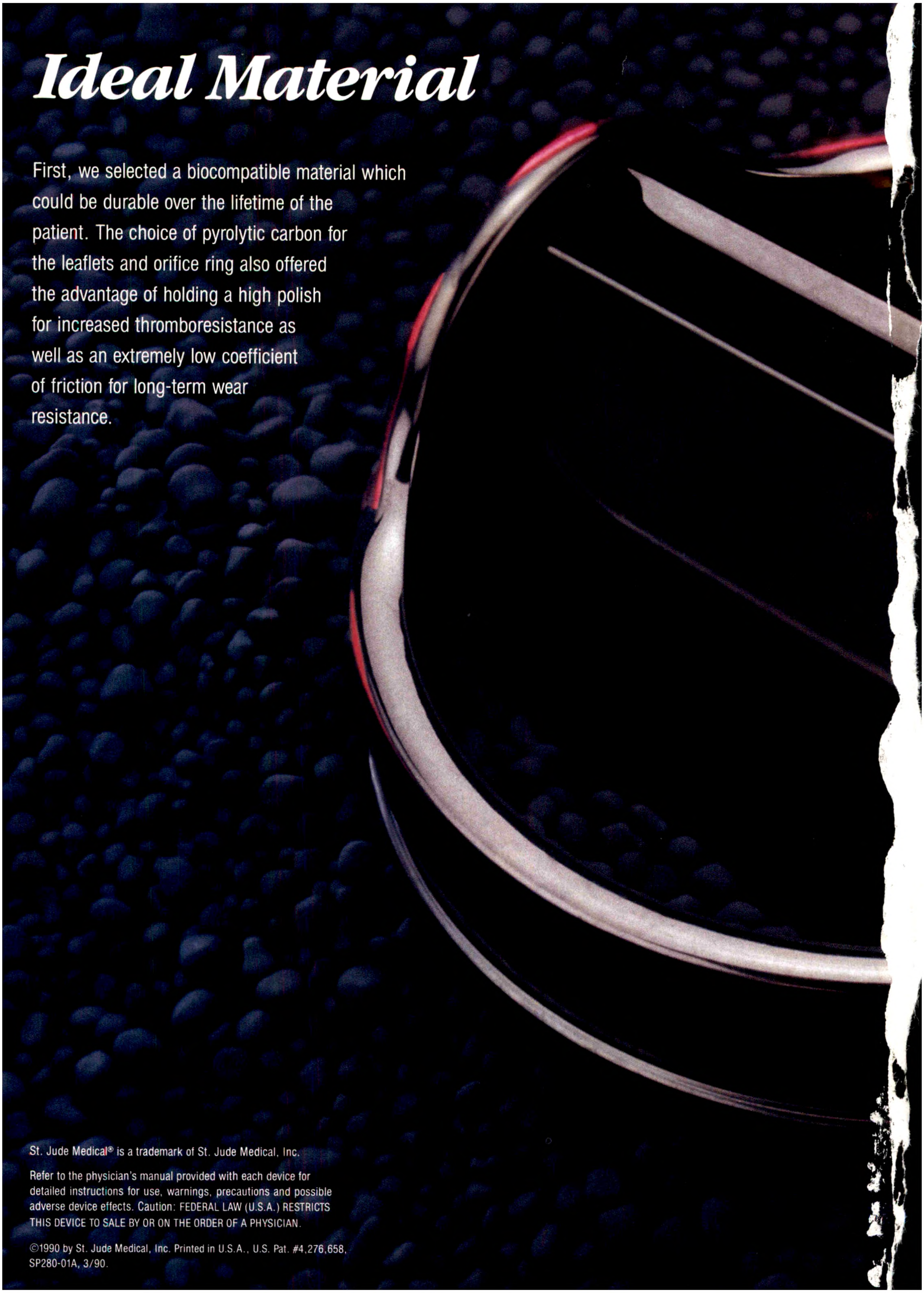

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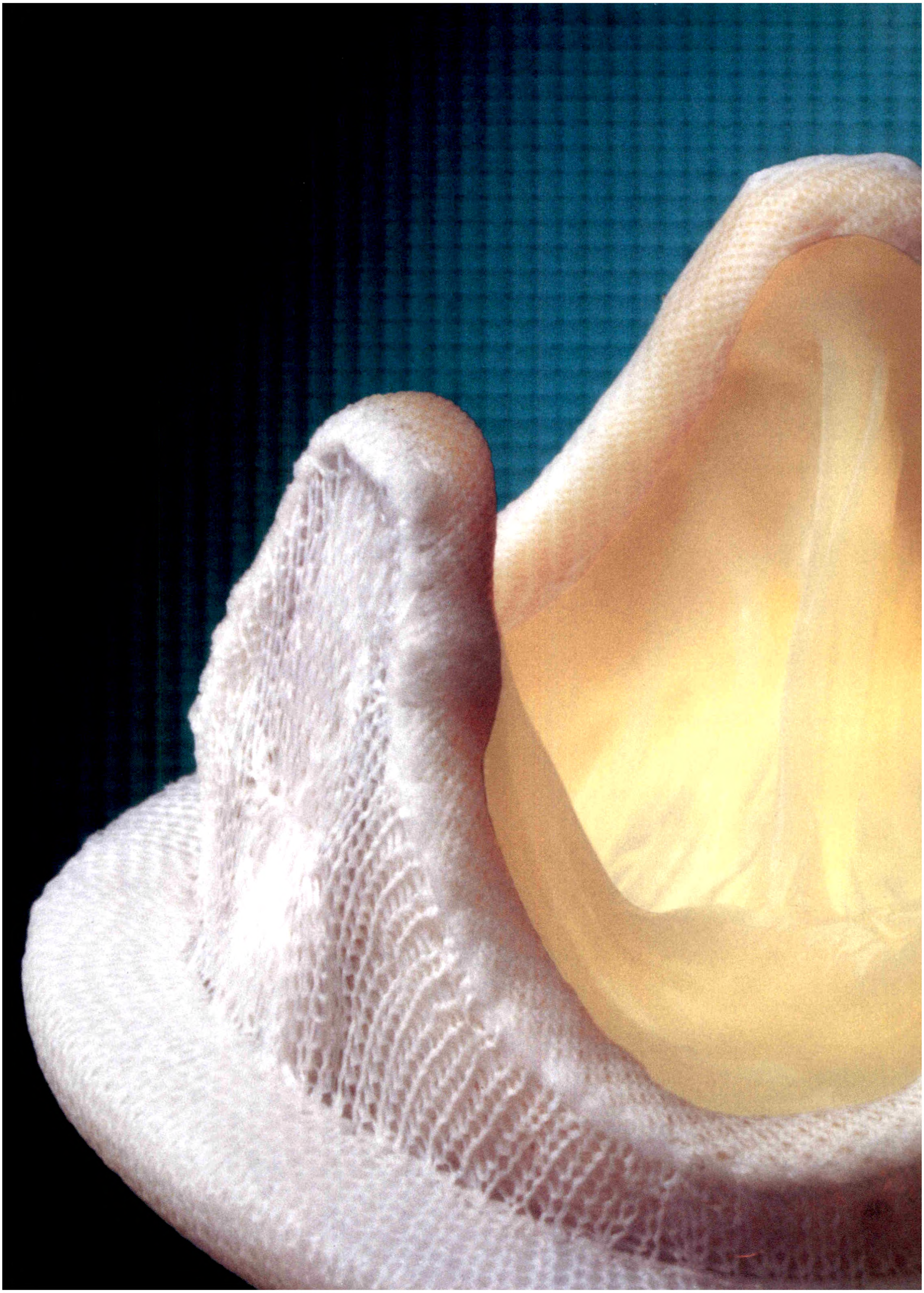

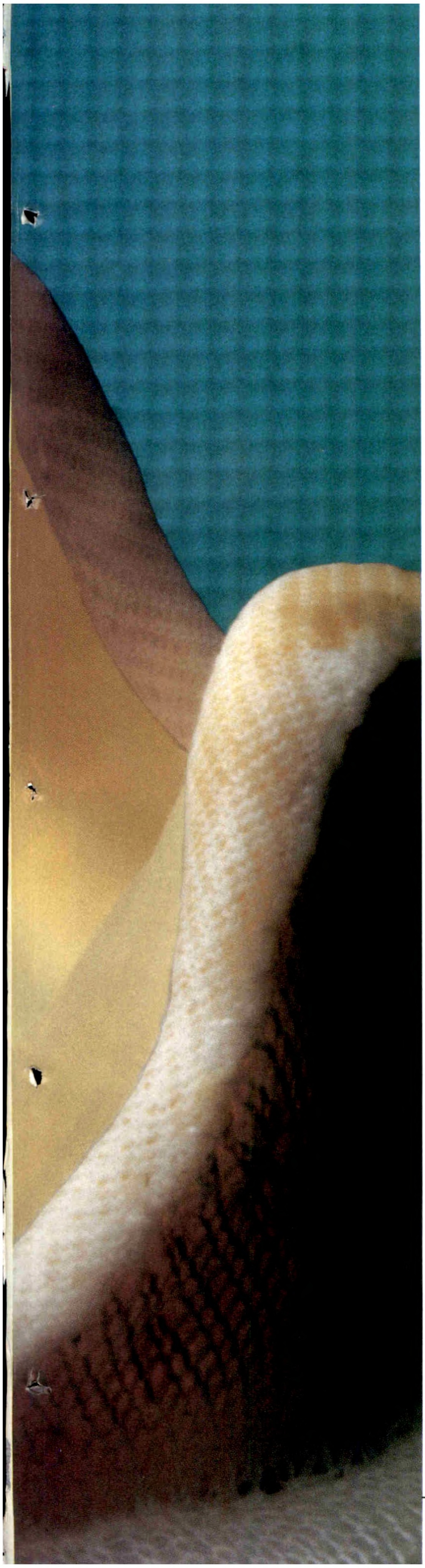

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Indications: Bioprostheses are indicated for use in patients suffering from valvular heart disease. Aortic and mitral valvular heart disease are conditions involving any of the following: obstructions of the heart valves, or stenosis; leakage of the valves, known as regurgitation or insufficiency; and combinations of the two, sometimes referred to as mixed disease or combined lesions. Valvular heart disease may be caused by any number of factors, including congenital abnormalities, infection by various microorganisms, degenerative calcification, rheumatic heart disease and rupture or dysfunction of the mitral subvalvular mechanism secondary to myocardial ischemia. Bioprostheses are used particularly in those patients for whom long-term anticoagulation is contraindicated or who may be difficult to maintain on anticoagulation therapy. The Carpentier-Edwards bioprosthesis is intended for use in patients whose aortic or mitral valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic or mitral valve prosthesis which is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. **Warnings:** For Single Patient Use Only In the presence of conditions affecting calcium metabolism or when calcium-containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients under 20 years of age, in patients on a high calcium diet, in the presence of severe systemic hypertension, and in patients who are on maintenance hemodialysis. The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile.** The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions: 1.** When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Carpentier-Edwards bioprostheses to calcification as compared to other commercially available porcine valves. **Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician. Baxter International Inc. is the owner of the following US patent which covers the products described herein: 4,106,129. Patent numbers in foreign countries supplied upon request. See package insert accompanying product for a full discussion of warnings, contraindications, complications and prescribing information. Carpentier-Edwards® is a registered trademark of Baxter International Inc.

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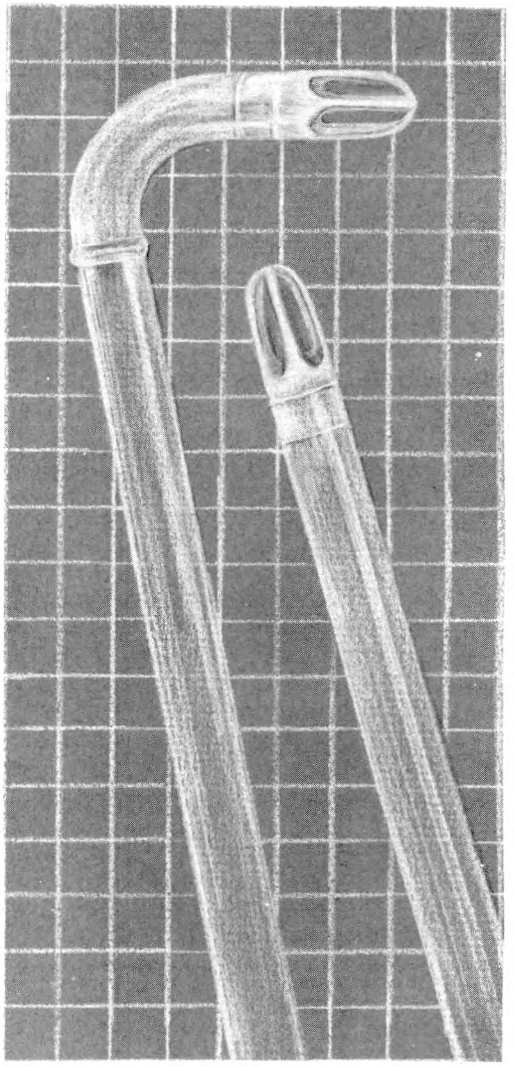

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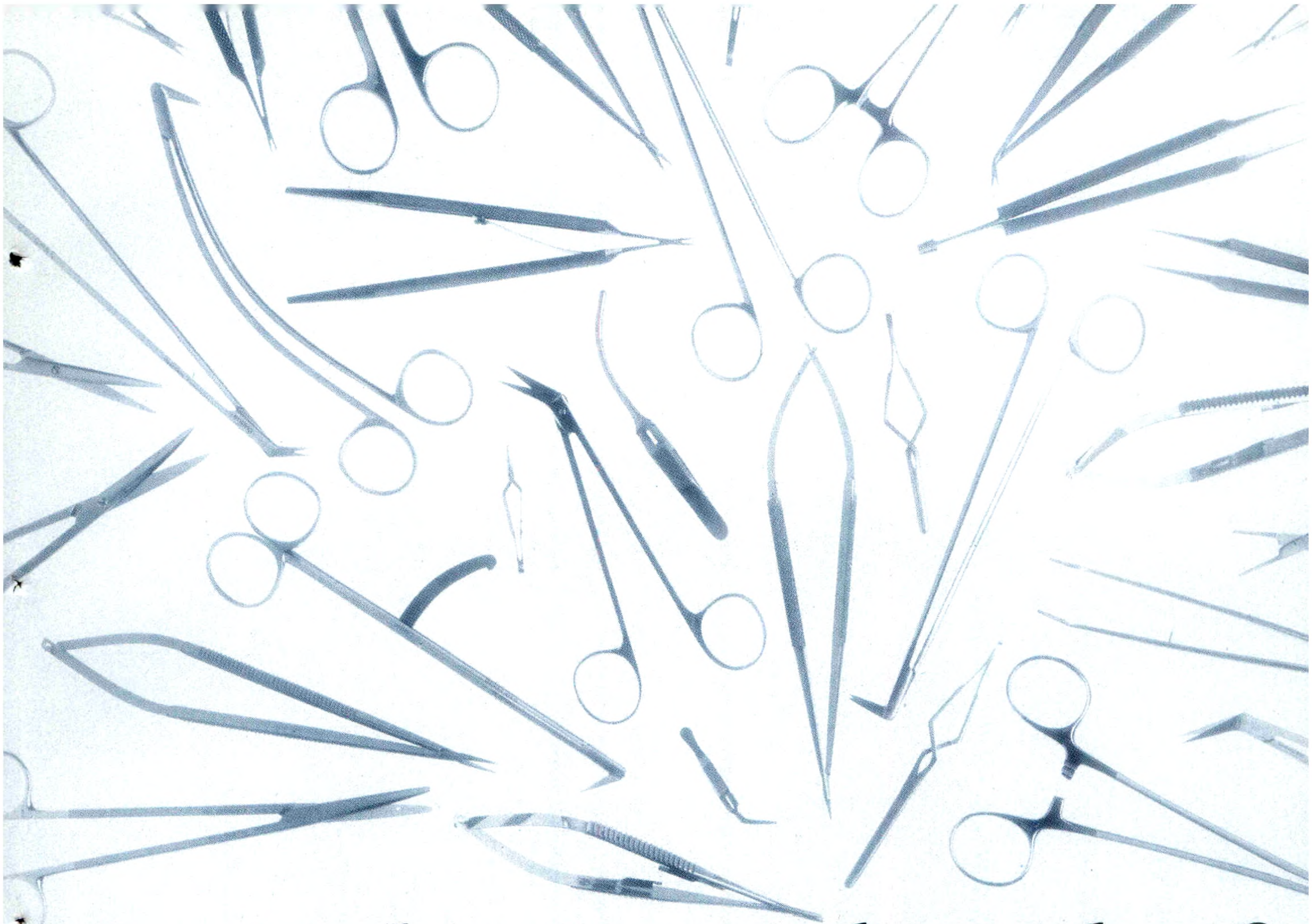

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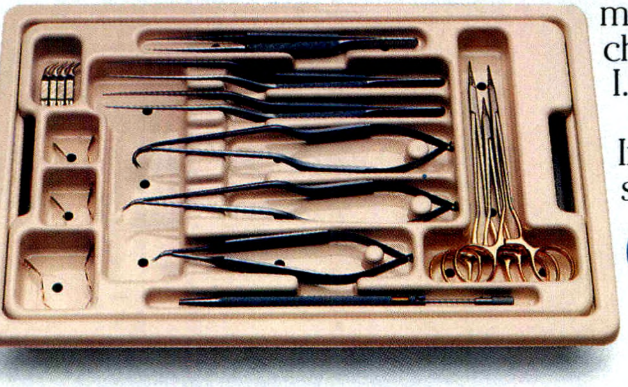

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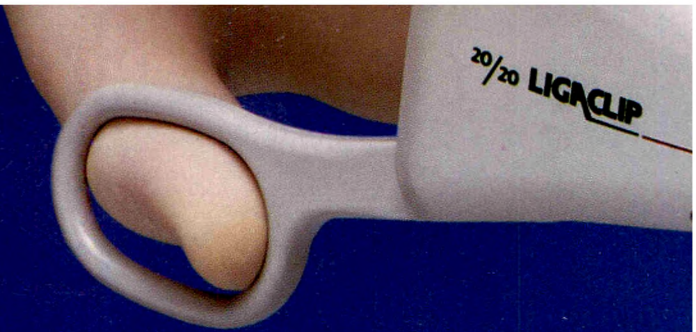

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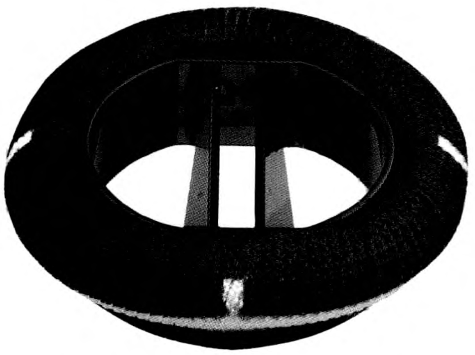

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Defining the Limits of Suitability of Cardiac Allografts

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In this issue, Sweeney and associates from the Texas Heart Institute [1] propose the use of "high-risk donor" (HRD) hearts for select critically ill recipients as a strategy to reduce the growing gap between cardiac allograft supply and demand. Their definition of HRD includes one or more of the following variables: age greater than 40 years, noncardiac systemic infections, cardiopulmonary resuscitation longer than 3 minutes, more than 5 hours of graft ischemia, recipient's weight more than 20% less than the donor's weight, and a requirement of more than 10 μg/kg/min of dopamine to maintain hemodynamic stability. Criteria for cardiac allograft donation established by the Stanford group [2] in the early 1970s were used for reference.

We agree with Sweeney and associates that the current shortage of donors is the most limiting factor to expansion of heart transplantation. The scarcity of suitable allografts makes the risk of dying while on the waiting list for a heart transplant (20% to 40%) greater than the operative risk or the risk of postoperative complications (10% to 20%) [3].

See also page 7.

The high success rate achieved in survival and quality of life after heart transplantation resulted in broadening of selection criteria for the recipient, leading to an even greater discrepancy between organ supply and demand. In addition, the lack of clear regional and national organ allocation policies makes the shortage of donors appear even worse.

Although the efforts of Dr Sweeney and his group to expand the cardiac donor pool seem appropriate and should be welcomed by the transplant community, an analysis of their HRD variables appears necessary. Rather than assuming donors older than 40 years to be high risk and those younger, low risk, it may be more appropriate to determine the biological age of the graft. Efforts should be made to obtain the donor's clinical history, particularly with respect to risk factors for coronary artery and rheumatic heart disease. Laboratory testing, including an echocardiogram, electrocardiogram, myocardial perfusion tests, and/or coronary angiography should allow a good assessment of ventricular function, cardiac anatomy, and myocardial perfusion. Such an approach has led our group to find "young hearts" in sexagenarian donors. It is hoped that in the near future "bench surgery" will yield "mended hearts" that would be an acceptable palliation for critically ill recipients. Informed consent would include knowledge of such graft manipulations, whenever possible.

In our experience, leukocytosis and hyperthermia in patients sustaining brain death do not necessarily correlate with sepsis. However, like Sweeney and associates, we have not observed a difference in heart transplantation outcome when donors with documented bacterial infections of the respiratory or urinary systems associated with positive blood cultures were used. Reliable serology tests should prevent the use of human immunodeficiency virus- or hepatitis-positive donors. Cytomegalovirus status is also important in determining the recipient's prophylactic therapy or careful monitoring for systemic cytomegalovirus infection.

Cardiopulmonary resuscitation of the donor and ischemia of 5 hours or more may be associated with myocardial ischemic injury. The clinical assessment and echocardiographic or angiographic studies currently used are not accurate enough to differentiate between reversible ischemic injury to the graft and necrosis. When serious necrosis is present before organ procurement, reperfusion injury may be observed after graft reimplantation. This phenomenon may account for at least part of the 10% operative mortality due to graft failure still reported worldwide [3]. Future clinical application of magnetic resonance imaging or positron emission tomography to the in situ donor's heart may help to differentiate between viable and necrotic myocardium.

Endocrine changes in patients suffering brain death are complex and not fully understood. However, we do know that reductions in 3,5,3'-triiodothyronine, thyroxine, plasma cortisol, and insulin are associated with changes from aerobic to anaerobic metabolism resulting in decreased donor myocardial function [4]. Electrolyte imbalances due to diabetes insipidus may be responsible for further diminution of myocardial performance. A better understanding of these metabolic disorders in brain-dead patients may lead to replacement hormonal therapy resulting in better preservation of myocardial intracellular structure and function.

Doctor Sweeney's group as well as other authors [5] consider a weight discrepancy between donor and recipient greater than 0.8:1 as another HRD criterion. Doctor Lower's group in the early 1970s [6] demonstrated long-term survival after orthotopic heart transplantation in

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dogs using donors as small as 30% of the recipient's weight. Mackenzie's group [7], as well as our institution, has been successful in using clinical cardiac allografts in the orthotopic position with a donor-recipient weight ratio of 0.5:1. A healthy graft as well as a recipient with normal pulmonary vascular resistance are important factors to be considered if smaller grafts are going to be used.

In conclusion, it may be appropriate to expand criteria applied to donors for cardiac transplantation, but efforts should be made to solve the problem of obtaining a more complete anatomical, functional, and metabolic assessment of the graft. Implicit to any plan that uses hearts approaching marginal acceptability is optimal procurement, surgical technique and storage, and careful manipulation of the graft after reperfusion. Highly sophisticated biochemical techniques should facilitate this effort. Perhaps perioperative administration of growth factors may accelerate the recovery of these biologically sound hearts.

The definition of HRD hearts is an evolutionary process. Retrospective analysis of large registries should allow contemporary risk-factor analysis techniques to identify specific criteria that correlate with poor graft outcomes. Such data would allow a more scientific definition of HRD, and the hypothesis could be tested with prospective registry inquiry.

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Surgical Standby for Coronary Angioplasty

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Peninsula Hospital, Burlingame, and University of California, San Francisco, California

The availability of skilled personnel, equipment, and facilities for emergency surgical revascularization has contributed importantly to the development and widespread clinical acceptance of catheter interventions on diseased segments of obstructed coronary arteries. Although sudden coronary occlusion requiring emergency coronary bypass grafting is infrequent after percutaneous transluminal coronary angioplasty (PTCA), a consensus exists among interventional cardiologists and cardiac surgeons that all PTCA procedures require surgical backup. The language adopted by the combined American College of Cardiology/American Heart Association Task Force on Guidelines for PTCA is unambiguous on this point:

> An experienced cardiovascular surgical team should be available within the institution for emergency surgery for all angioplasty procedures. The Subcommittee feels strongly that there should be no exception to this requirement and holds the position that all arrangements requiring the transportation of patients to off-site surgical facilities for such emergency surgery fails to meet the necessary standards of care exercised by prudent physicians and cannot be condoned [1].

One of the implications of this consensus is that vast resources must be committed to supporting catheter-intervention technology in order to minimize acute complications in approximately 5% of patients. In 1988, the most recent year for reliable data, 227,000 patients underwent coronary angioplasty in this country. The same year 254,000 patients underwent coronary artery bypass grafting (National Center for Health Statistics, 1988 Hospital Discharge Survey; personal communication, March 1990).

See also page 35.

The survey reported by Cameron and co-authors [2] gives an up-to-date look at various ways surgical standby for PTCA is provided in this country. As the survey did not attempt to include outcome data it is impossible to decide which, among the several strategies, is optimal. Given the variety of ways cardiovascular services are provided in this country it would be surprising if a consensus existed about an optimal standby strategy. We learn that a substantial majority of institutions provide a "formal" standby arrangement (64% of institutions responding to the survey maintain an open operating room). Nearly one third modify their usual standby arrangements for unusual, high-risk cases. Again, lacking outcome data we cannot know whether assigning priority to patients according to levels of anticipated risk, and providing corresponding levels of standby-readiness, gives results comparable with the "operating-room-held-open-for-all-patients" policy.

Cameron and co-authors point out that recent papers addressing the cost of PTCA versus the cost of coronary artery bypass grafting fail to include the costs of surgical standby, which are often not compensated and are borne indirectly by all cardiac surgical patients or by all hospital patients. These costs are substantial. Wilson and associates [3], reporting their PTCA standby experience (699 patients undergoing PTCA from November 1980 to May 1985 in which an operating room was held open for all patients), found actual costs determined by standard accounting methods to be $1,188,843.00 for the series or $1,700.00 per angioplasty attempt. A rough estimate for 1988 (227,000 PTCA's × 64% formal standby × $1,700.00) yields $246,976,000.00 for only a portion of standby services, exclusive of the remaining 36% covered by other standby strategies, the costs of which are not known.

A more subtle effect of the national policy (ACC/AHA guidelines) to provide surgical cover for all patients undergoing PTCA is the stimulus to create new cardiac surgical programs in order to support angioplasty activity in hospitals with new or free-standing catheterization laboratories heretofore content to refer patients to established centers for angioplasty and surgery [4]. The proliferation of low-volume cardiac surgical programs whose primary raison d'être is to provide surgical standby for PTCA raises quality and cost issues perhaps not anticipated by the ACC/AHA Task Force and adds substantially to the costs of providing PTCA services in this country. A recent paper from Great Britain reporting a PTCA standby experience in the "next-available-operating-room" mode describes a practice in which patients requiring emergency surgical revascularization are transported to a nearby (2.4 km) cardiac surgical center with, according to the authors, acceptable outcomes in patients carefully selected for PTCA [5]. Bonchek [6] recently raised this issue for debate in this country.

Suffice it to say that notwithstanding the benefits of emergency surgical intervention in a small fraction of patients undergoing PTCA, omnipresent surgical standby is inefficient and expensive. I agree with Cameron and co-authors that the actual costs of surgical standby for PTCA must be brought into the sunlight if the costs of PTCA, which continues to be touted as a less expensive alternative to coronary bypass grafting, are to be fully appreciated.

Six prospective trials are currently underway compar-

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ing PTCA versus medical treatment (ACME)* and PTCA versus surgical revascularization (BARI, CABRI, EAST, GABI, RITA)†. All will collect cost data. One prays that the costs of surgical standby will be included in these analyses. When the time-related freedom from untoward outcome events and the associated costs of these events for PTCA compared with alternative management strategies become known, we will have a better notion of the place of PTCA in the therapeutic armamentarium for patients with ischemic heart disease.

The survey by Cameron and co-authors stimulates us to consider the interface between cardiologists and cardiac surgeons in providing catheter interventions in patients with coronary heart disease. It is clear that our strategies for protecting patients undergoing PTCA from untoward outcomes are still evolving. Perhaps better patient selection and technological innovation including bail-out catheters, intraluminal stents, and circulatory support devices will provide more efficient and less costly alternatives to current standby practices.

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* ACME = Angioplasty Compared to Medicine.

† BARI = Bypass Angioplasty Revascularization Investigation; CABRI = Coronary Angioplasty versus Bypass Revascularization Investigation; EAST = Emory Angioplasty Surgery Trial; GABI = German Angioplasty Bypass Investigation; RITA = Randomized Intervention Treatment of Angina.

Bronchial and Thymic Carcinoids and the Ectopic ACTH Syndrome

William D. Odell, MD, PhD

Bronchial adenoma or carcinoid is a relatively rare cause of so-called ectopic ACTH (adrenocorticotropic hormone) syndrome and comprises approximately 2% of all causes of ectopic ACTH production [1]; carcinoid syndrome also occurs with only about 2% of such neoplasms [2]. Approximately 10% of patients with ectopic ACTH syndrome have carcinoma or carcinoid of the thymus [1]. These tumors are of great interest as a cause of this condition because differentiating them from the pituitary gland as the source of ACTH is particularly difficult.

Forty to 50% of patients with bronchial carcinoid and ectopic ACTH syndrome show suppression of ACTH and cortisol with high-dose dexamethasone treatment, a finding usually indicating pituitary-dependent ACTH secretion (Cushing's disease). This finding suggests that some bronchial carcinoids may secrete corticotropin-releasing hormone (CRH), which in turn stimulates pituitary secretion of ACTH. As dexamethasone and other glucocorticoids act directly on the pituitary to inhibit CRH action, the "ectopic" CRH syndrome is expected to show dexamethasone suppression. In such cases, petrosal venous sampling would be expected to show an ACTH gradient over peripheral blood and would not therefore distinguish bronchial carcinoid from Cushing's disease. Malchoff and associates [3] have reported that both dexamethasone suppression and CRH stimulation testing of a patient with bronchial carcinoid and Cushing's syndrome gave results typical of Cushing's disease. In addition, plasma ACTH concentrations are usually very highly elevated in ectopic ACTH syndrome, which distinguishes the usual patient with ectopic ACTH from one with Cushing's disease, in which ACTH concentrations are normal or only slightly elevated. However, in ectopic ACTH syndrome caused by bronchial carcinoids, the plasma ACTH concentrations are usually only slightly elevated—mimicking Cushing's disease. Howlett and coworkers [4] presented data on 6 patients with bronchial carcinoid and 2 with thymic carcinoid, all with ectopic ACTH syndrome. Plasma ACTH level ranged from 15 to 54 pmol/L (69 to 244 pg/mL) in these 8 patients (normal, 2 to 18 pmol/L). Patients with Cushing's disease had plasma ACTH ranging from 9 to 94 pmol/L (42 to 428 pg/mL). Just as it is often metabolically difficult to distinguish bronchial carcinoid-ectopic ACTH from pituitary-dependent Cushing's, it is also difficult to detect bronchial carcinoids because they are usually very small tumors. Zarate and associates [5] have published the case of a young girl with Cushing's syndrome who had a pituitary adenoma. This was removed but showed no immunostaining for ACTH, and Cushing's syndrome persisted after adenoma removal. The patient died and autopsy showed a bronchial carcinoid immunostaining for CRH and ACTH. Possibly the CRH stimulated adenoma formation, or alternatively the adenoma was incidental.

See also pages 52 and 58.

Data from a number of laboratories including our own [6] have demonstrated that the precursor ACTH molecule, proopiomelanocortin (POMC) is extractable from all normal human and rat tissues as well as all carcinomas from patients without Cushing's syndrome. This POMC-like molecule was shown to have no biologically active ACTH-like activity as assessed by in vitro adrenal cell assays. However, when exposed to trypsin, a biologically active ACTH with an expected molecular weight of 4,500 was produced. We also showed that this precursor ACTH molecule circulates in plasma in patients with a variety of carcinomas, but who do not have Cushing's syndrome. Those patients having Cushing's syndrome from ectopic ACTH production have neoplasms that convert this POMC to biologically active ACTH. It is in this context that we believe the so-called ectopic ACTH syndrome is not ectopic [1, 6].

In this issue, Pass and associates [7] review experience with 13 patients with bronchial and 1 patient with thymic carcinoid causing Cushing's syndrome. Regrettably, they do not present data on the fraction of patients who showed dexamethasone suppression, although all patients underwent high-dose dexamethasone suppression tests. These patients also underwent CRH stimulation, a test that typically shows a brisk stimulation of ACTH secretion in Cushing's disease. None of the 14 patients tested responded to CRH, a finding strikingly in favor of ectopic ACTH syndrome, but as reviewed, a finding not always seen in bronchial carcinoid-ectopic ACTH syndrome. Petrosal vein sampling for ACTH also revealed no step-up of ACTH concentrations over peripheral vein in these 14 patients.

The review of Pass and associates demonstrates how effective operation coupled, when appropriate, with postoperative mediastinal irradiation results in a very high cure or remission rate. Twelve of 14 patients undergoing operation were alive at a mean of 21 months postoperatively and cortisol concentrations were normal in 10 of the patients. Adrenocorticotropic hormone and cortisol are excellent tumor markers in these patients and it is possible, even though time from onset of disease to correct

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diagnosis is often years, that the tumors when detected are smaller than for nonfunctioning bronchial carcinoids.

Also in this issue, Economopoulos and co-workers [8] review their experience with 7 patients with thymus carcinoid. These carcinoids apparently were not functioning; none produced ACTH. The mortality of these patients was considerably greater than that of the patients described by Pass and associates. All but 2 died 1 to 12 years after operation and irradiation treatment. It would appear from these two studies that the nonfunctioning thymus carcinoids are considerably more aggressive neoplasms than the ACTH-secreting bronchial carcinoids. Ectopic ACTH syndrome caused by "carcinoma" of the thymus accounts for about 10% of cases of ectopic ACTH syndrome. This classification should be reviewed with modern histological techniques to distinguish thymus carcinoid from carcinoma.

The data of Pass and associates on 13 patients with bronchial carcinoid are of major interest. The findings of great reliability in excluding Cushing's disease by petrosal vein sampling for ACTH and the failure of CRH to stimulate ACTH are somewhat surprising in view of scattered patient reports suggesting otherwise and also in view of the suppression of ACTH/cortisol production by high-dose dexamethasone in 40% to 50% of other reported patients with bronchial carcinoid. The excellent response to operation and tumor therapy is particularly gratifying to read.

Finally, it is important to note that increasingly ACTH is being measured by immunoradiometric or sandwich type assays [9]. The precursor molecule(s) of ACTH that are produced by at least some patients with ectopic ACTH syndrome may not react in these assays giving a misleading low value for ACTH. As always the clinician must be particularly alert to distinguish these disorders.

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Extension of Donor Criteria in Cardiac Transplantation: Surgical Risk Versus Supply-Side Economics

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To combat the continuing shortage of ideal donor hearts, we have used cardiac allografts from high-risk donors for critically ill recipients. We defined high-risk donor variables as age greater than 40 years, systemic (noncardiac) infection, cardiopulmonary resuscitation greater than 3 minutes, ischemic time longer than 5 hours, weight more than 20% less than that of the recipient, and requirements for high doses of inotropes. Of the 305 donors we have used, 73 (23.9%) have been high-risk, with 59/73 (80.8%) exhibiting one variable, 12/73 (16.4%) exhibiting two variables, and 2/73 (2.7%) exhibiting three variables. No correlation was found between the number of donor variables and a poor postoperative result. No infectious complications occurred in 17 patients receiving hearts from potentially infected donors. Hospital mortality rates (30 day) for recipients of high-risk donor versus non–high-risk donor hearts were 8.2% and 6.9%, respectively (not significant). The 1-, 6-, and 12-month actuarial survival rates were 91.7%, 81.2%, and 75.9% for the high-risk donor group and 93.5%, 80.3%, and 77.8% for the non–high-risk donor group (not significant). Among survivors with high-risk donor hearts, mean left ventricular ejection fractions were 0.54 ± 0.08 at 3 months, 0.55 ± 0.08 at 1 year, and 0.54 ± 0.09 at 2 years after transplantation. These results suggest that accepting less than ideal donor hearts can be safe and might be considered when better options are not available.

(Ann Thorac Surg 1990;50:7–11)

Cardiac transplantation has become a widely accepted and regularly used method for treating certain patients with heart disease. When the pioneers of the late 1960s demonstrated the feasibility of human heart transplantation, many other centers initiated programs of their own, and the recent era has witnessed a virtual explosion in both the evolution of this specialty and the numbers who choose to practice it. Progress has also been made in understanding more of the intricacies of the rejection process, and this progress has practically moved the center stage from the operating rooms to the immunology laboratories [1–3].

For editorial comment, see page 1.

Among the problems facing the majority of today's cardiac transplant teams, none is more vexing (or potentially more restrictive) than the continuing shortage of ideal donor hearts. Standard donor criteria were originally established, perhaps appropriately, without an understanding of the impact modern therapies would have in bringing more and sicker patients to an expanding number of recipient waiting lists [4]. In confronting the disparities in demand and supply in our own program, we have on occasion liberalized the standard donor criteria and accepted less than ideal donor hearts for critically ill recipients. This unorthodox strategy has produced surprisingly good results to date. Our experience confirms that this practice can be efficacious, saves both lives and money, and may deserve consideration for application in other programs.

Material and Methods

The hospital records and follow-up donor charts of 305 orthotopic cardiac transplant recipients who were operated on at the Texas Heart Institute between July 1982 and March 1989 were reviewed. For the purpose of this review, recipients of both heterotopic and retransplant operations were excluded, as we wished to focus on the performance of hearts from high-risk donors. Of the 305 patients, 232 (76%) received cardiac allografts from non–high-risk donors (NHRD) who met the standard selection criteria, whereas 73 patients (24%) received hearts from donors who were deemed high-risk (HRD) because of their failure to meet the standard benchmarks of "safe" donor status. The overwhelming majority of these 73 critically ill patients, who were terminally hospitalized or bedridden at home, received HRD hearts because of their extremely poor prognosis. Demographic data from both HRD and NHRD groups are shown in Table 1.

High-risk donor variables were defined as one or more of the following: age greater than 40 years, systemic

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Table 1. Demographic Data of Transplant Recipients

Variable	HRD	NHRD	p Value
Male	55 (75.3%)	201 (86.8%)	NS
Female	18 (24.7%)	31 (13.2%)	NS
Age	46.3 yr (7 mo to 67 yr)	47.4 yr (4–68 yr)	NS
Donor age	27.1 yr (2–53 yr)	24.4 yr (8–39 yr)	NS
Follow-up	19.4 mo (2 days to 59 mo)	22.9 mo (4 days to 84 mo)	NS

HRD = high-risk donor; NHRD = non–high-risk donor; NS = not significant.

(noncardiac) infection, cardiopulmonary resuscitation longer than 3 minutes (less than 10 minutes), ischemic time more than 5 hours, weight more than 20% less than that of the recipient, and requirements for high doses of inotropes after volume reexpansion (eg, >10 μg/kg/min of dopamine or >5 μg/min of epinephrine). Systemic (noncardiac) infections were defined by multiple (more than two) positive blood cultures, leukocytosis ($>20 \times 10^9$/L [20,000/μL]) in conjunction with a temperature of greater than 38.9°C rectally, and radiographic evidence of pulmonary infiltrates with documented positive sputa. At the time of donor cardiectomy, these hearts were inspected to confirm the absence of valvar vegetations, myocardial abscesses, or frank pus. Recipients were also categorized as to whether their HRD graft exhibited one, two, or three of the HRD variables. Fifty-nine patients (81% of the HRD group) received hearts from donors with a single HRD variable, 12 patients (16% of total HRD group) had two-HRD-variable hearts, and 2 patients received three-HRD-variable hearts. Table 2 shows HRD-group recipients according to number and type of variables.

In the cohort aged more than 40 years, 9 were single-HRD-variable (aged >40 years only) and 3 were multiple-HRD-variable donor hearts. Ages ranged from 42 to 53 years in these donors, and all were men. Only 3 of these 12 donors received a cardiac catheterization before cardiectomy, but all 12 had normal bedside echocardiograms and were without evidence of coronary insufficiency according to preharvest electrocardiography. Similarly, the 12 total donors who required cardiopulmonary resuscitations of more than 3 minutes (9 as their only HRD variable) had hearts that were functioning without objective evidence of ischemic damage before cardiectomy. None of these patients underwent cardiac catheterization.

Sixteen donors were included because of a body weight of more than 20% less than that of the recipient (range, 20% to 31%). Of these, 8 had weight mismatch as their only inclusion criterion. Seven donors had this as one of two HRD variables, and 1 donor with three HRD variables weighed more than 20% less than the respective recipient. In each recipient in this category, care was taken to ensure an absence of elevated pulmonary vascular resistance before using a heart from an undersized donor. Donors who required high-dose inotropic support before cardiectomy included 21 single-HRD-variable, 8 double-HRD-variable, and 2 triple-HRD-variable patients. These 31 total donors, who needed high-dose dopamine (21 patients), epinephrine (9 patients), or both (1 patient) represented our most common deviation from the accepted NHRD criteria. A lengthy ischemic time dictated the inclusion of only 1 patient (a two-HRD-variable donor).

Systemic (noncardiac) infections were involved in 17 total HRD patients, 12 as a single-HRD-variable, 4 as a double-HRD-variable, and 1 as part of a triple-HRD-variable donor. Of these 17 donors, 7 had multiple positive blood cultures: *Streptococcus pneumoniae* (3), *Staphylococcus aureus* (2), *Klebsiella pneumoniae* and *Enterobacter sp* (1 each). Nine other donors were accepted despite temperatures of more than 38.9°C in conjunction with leukocytosis ($>20 \times 10^9$/L [20,000/μL]) and pulmonary infiltrates with positive sputa (*Enterobacter*, 3; *Klebsiella pneumoniae*, 3; *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Hemophilus influenzae*, 1 each). The 1 remaining donor was used despite documented hepatitis B surface antigen positivity.

Statistical analyses were performed using the unpaired Student's t test, χ^2 analysis, and the Mantel-Haenszel test for life-table analysis.

Results

Follow-up for HRD recipients averaged 19.4 months (range, 2 days to 59 months) compared with 22.9 months (range, 4 days to 84 months) in NHRD recipients (not significant). Overall mortality rates were similar for the HRD and NHRD groups, manifesting no statistical difference at 1, 6, 12, and 24 months. Survival curves for each group are shown in life-table form in Figure 1. Twenty of the HRD recipients ultimately died; 14 of these were late deaths that occurred after discharge from the hospital (range, 30 days to 4.5 years). Of these 14 late deaths, six were due to infections (three viral, two bacterial, and one protozoan), three resulted from graft atherosclerosis (none from donors aged >40 years), and two each resulted from uncontrolled rejection or hepatorenal insufficiency. The remaining late death resulted from hemorrhage after a liver biopsy on day 65 in the patient whose

Table 2. High-Risk Donor Group by Number and Type of Variable (n = 73)

One HRD Variable (n = 59)	Two HRD Variables (n = 12)	Three HRD Variables (n = 2)
Ino 21	Ino/Wt 3	Ino/Age/Inf 1
Inf 12	Ino/Inf 2	Ino/Age/Wt 1
CPR 9	Wt/Inf 2	
Age 9	Wt/CPR 2	
Wt 8	Ino/Age 1	
Isc 0	Ino/CPR 1	
	Ino/Isc 1	

Age = age >40 yr; CPR = cardiopulmonary resuscitation; HRD = high-risk donor; Inf = infection; Ino = inotrope; Isc = >5 h of ischemic time; Wt = weight $>20\%$ less than that of recipient.

transplant was from the hepatitis-positive donor. (The biopsy was negative.)

Six HRD recipients died early in the postoperative period (range, 17 to 29 days) before discharge from the hospital. HRD variable(s) and causes of death in these 6 patients are shown in Table 3. One of these patients had received a heart from a donor with positive blood cultures for *S aureus* but died on day 20 of sepsis from *Pseudomonas aeruginosa* (without evidence of *S aureus*). The three-HRD-variable donor underwent transplantation early in our series, and an early death resulted from drug-induced hepatic failure.

Four HRD patients required 48 to 96 hours of postoperative mechanical support with a right ventricular assist device (2 patients), an intraaortic balloon pump (1 patient), or a left ventricular assist device (1 patient). Three of these had high-dose inotropic support of the donor as their only HRD variable, and 2 of these 3 died (1 early, 1 late). The remaining patient was included in the HRD group because of a donor age of 49 years. Although this donor underwent cardiac catheterization and was accepted, the heart performed poorly after transplantation and needed 48 hours of support with a centrifugal pump right ventricular assist device. This patient was weaned from support and remains alive and well 17 months later.

An analysis of the impact that the number of HRD variables had on recipient survival shows no difference between the one-HRD-variable and two-HRD-variable groups, especially during the early, predischarge period when HRD variables would probably have their greatest effect. Fifteen of 59 one-HRD-variable recipients died (4/59 early deaths), and 3 of 12 two-HRD-variable recipients died (1/12 early deaths). Both three-HRD-variable recipients died (1 early, 1 late), but this sample was too small to have statistical validity.

No single donor variable could be shown to have value in predicting a poor postoperative result. The need for high-dose inotropic support of the donor heart was a frequent HRD variable in both the six early deaths in our HRD series and the 4 patients who required mechanical support postoperatively, although this frequency did not achieve significance because of the small numbers involved. No HRD recipient included in the series as a result of donor infection died from or became infected with the organism identified in the donor. One patient received a one-HRD-variable heart from a 47-year-old donor (studied angiographically) that demonstrated severe atherosclerosis in the proximal left anterior descending coronary artery. At transplantation, a left internal mammary artery to left anterior descending coronary artery bypass graft was created as part of the procedure, and the patient continues to do well 6 months later.

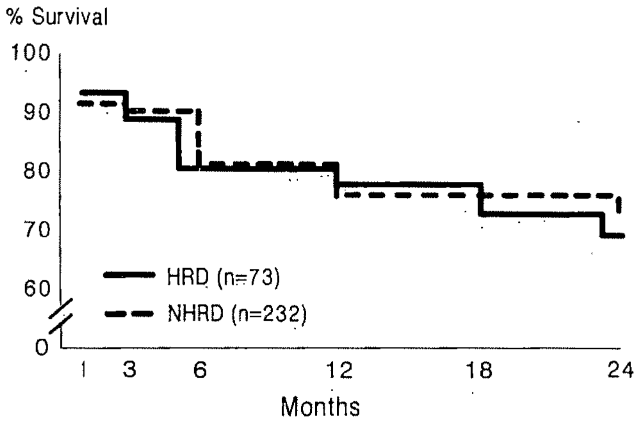

Fig 1. Actuarial survival in transplant patients who have received hearts from high-risk donors (HRD) *and non–high-risk donors* (NHRD).

Table 3. Early (in-Hospital) Deaths in HRD Recipients

HRD	Cause of Death	n
Ino	Infection[a,b]	2
Ino	Neuro. deficit	1
Inf[c]	Infection[a]	1
Ino/Inf	Rejection	1
Ino/Age/Inf	Liver failure	1

[a] *Pseudomonas aeruginosa*; [b] Cytomegalovirus; [c] *Staphylococcus aureus.*

Age = age >49 yr; HRD = high-risk donor; Inf = infection; Ino = inotrope.

Our routine posttransplantation protocol involves serial determinations of left ventricular ejection fractions through gated blood pool studies. Among survivors, there was no significant difference between HRD and NHRD recipient ejection fractions. At 3, 12, and 24 months, HRD recipients had a mean left ventricular ejection fraction of 0.54 ± 0.08, 0.55 ± 0.08, and 0.57 ± 0.09, respectively, and NHRD recipients showed a mean left ventricular ejection fraction of 0.56 ± 0.10, 0.57 ± 0.09, and 0.60 ± 0.08, respectively.

Comment

Recent data from the Registry of The International Society for Heart Transplantation show that 2,450 cardiac transplant operations were performed worldwide in 1988, an increase of 450 since 1986 and of only 250 since 1987. At least one major reason for this general slowing of activity may be the limited numbers of acceptable cardiac donors available when standard donor criteria are used. During this same period, the number of cardiac transplant centers increased from 100 in 1985 to 173 in 1988, and the average length of time that potential recipients must wait for a donor heart may reach 3 to 6 months in some regions [5]. Simultaneously, we have perceived a trend toward referral of an increasing percentage of high-risk patients for transplantation at the Texas Heart Institute. Although 5% and 7% of our 1986 and 1987 patients were listed as what is now defined by the United Network for Organ Sharing as status 1, 12% of the patients in 1988 were listed as status 1 before their transplantation. Moreover, the average waiting period for such recipients has been steadily increasing in our center because of a relative shortage of NHRD hearts and is currently approaching 3 months. Of the 166 patients we listed in 1988, 42 (25%) died while waiting for a donor heart, a figure that appears to be depressingly predictable based on reports from other centers [6, 7].

The hospital-related costs for cardiac transplantation have been reported to be in the range of $50,000 to $100,000 [8, 9], but little has been made of the costs associated with dying in the hospital while waiting for a cardiac donor. A review of the last year in our institution shows an average cost of $56,078 (range, $33,104 to $77,181) for status-1 patients who died, despite pharmacological or intraaortic balloon pump support, waiting for a donor heart. Although we support the continued progress being made with more sophisticated mechanical device "bridging" of status-1 patients, such patients can be assumed to incur in-hospital costs in amounts equal to or greater than those described because they require postventricular assist device stabilization before transplantation [10].

We are thankful, and in some cases surprised, that our results with HRD hearts have been good to date. In particular, patients receiving hearts from potentially infected donors have manifested few infectious complications, and none had the same infecting agent identified in the respective HRD donor. In addition, the lack of any difference in short- or long-term results between one-HRD-variable and two-HRD-variable hearts is of interest. Although both three-HRD-variable recipients ultimately died, 1 of these, early in our series, was an in-hospital death secondary to drug-induced hepatic failure and the other was a late death (2 months after transplantation) resulting from cytomegalovirus infection and probably not related to the performance of the HRD heart. Although a requirement for high-dose inotropic donor support failed to achieve significance as an HRD variable, this donor condition was associated with several poor postoperative results and deserves further attention. Our lack of donor hearts from the group with long ischemic time (only 1 patient) is perhaps most symbolic of the general problem. Rather than any lack of interest in such donors on our part, this may reflect the competitive element of garnering cardiac donor populations in an era of more transplant centers with an unchanging donor supply.

Are there any donor hearts that should not be used? Clearly the answer is yes. During the past year, we have continued to refuse donor hearts traumatized as a result of blunt or penetrating injury, and we do not recommend use of small hearts in the orthotopic position when the recipient pulmonary pressures and resistances are high. We have generally avoided hearts from older donors with known ischemic heart disease, but aortocoronary bypass grafting can be performed on these donor hearts as part of the orthotopic transplant procedure, and this may be attempted more often in the future. Last, many HRD hearts that are not suitable for use in the orthotopic position might conceivably be placed heterotopically and function as both an allograft and a ventricular assist device, without the need to assume the entire burden of circulatory support.

Standard donor criteria are logical and safe and have served cardiac transplant surgeons and their patients well for many years. On occasion, however, these criteria might be carefully extended in addressing a mismatch between supply and demand. Our experience indicates that such a strategy may be appropriate for certain recipients and, when prudently applied, may result in saving both lives and money.

We thank the Department of Biostatistics and Computer Applications for statistical analyses in this study.

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DISCUSSION

DR SHREEKANTH KARWANDE (Salt Lake City, UT): Doctor Sweeney and his associates have made a very valid observation, that the availability of donor hearts is the primary limiting factor to the number of cardiac transplantations that can be done. When public awareness and education, along with local and regional organ donation policies, have achieved their maximum expected returns, we must seriously look at liberalizing the donor criteria as the only means of increasing the number of organs available for transplantation.

From its very beginning, at the Utah Cardiac Transplant Program we have used two-dimensional echocardiography as a routine screen for potential donor hearts. This is a noninvasive test that is available in most hospitals and, generally speaking, there is a cardiologist who is more than willing to analyze the study.

Between March 1985 and September 1989, 286 donor hearts were screened by two-dimensional echocardiography. Of these, 34, that is, 12%, were rejected based on echocardiographic findings, and only two that were acceptable by echocardiography were rejected at the time of organ recovery by means of visual inspection. Eighty-three, which is 29% of these hearts, fell into the high-risk group as identified by Sweeney and associates, but these were acceptable for transplantation by echocardiographic criteria.

The majority of these hearts were from donors who required high doses of inotropes and vasopressors, but some were also from donors who had suffered trauma and periods of cardiac arrest.

The acceptable echocardiographic findings are mild septal hypokinesis, mild degrees of mitral regurgitation, and small amounts of pericardial effusion.

The hearts rejected for transplantation by echocardiographic criteria have had global hypokinesis, severe septal hypokinesis, or serious mitral and tricuspid valve insufficiency. Of the two hearts acceptable by echocardiography but rejected by direct inspection, one had severe right ventricular dilatation and hypokinesis and the other had serious myocardial contusion without any demonstrable dysfunction of the heart itself.

In addition to two-dimensional echocardiography, we also perform coronary arteriography on all potential male donors who are more than 40 years old and female donors more than 45 years old. We use crystalloid cardioplegia in a single 1-L dose and have experienced ischemic times ranging from about 50 minutes to 6½ hours. There have been no intraoperative deaths in the recipients receiving these high-risk hearts.

Only 1 patient died of normal cardiac causes. For recipients with elevated pulmonary vascular resistance, however, we have made a conscious effort to get a perfect heart and also have predictably short ischemic times.

We have identified two groups of donors that we are very worried about. The first is patients who have been exposed to carbon monoxide. These donor hearts have a tendency to develop fatty infiltration and pump failure. The second group is patients with severe head injury requiring high-dose inotropic support in spite of volume expansion. Serial echocardiograms in these patients have demonstrated a decrease in ventricular function.

I have several questions for Dr Sweeney. Have you made any effort to match these high-risk hearts with recipients who fall into various risk strata, such as hearts from older donors to be placed in older recipients, or hearts from high-risk donors being preferentially used for patients with low pulmonary vascular resistance, or hearts from high-risk donors being acceptable for UNOS status 1 patients but being refused for status 2 patients? Have you used two-dimensional echocardiography as a screening modality in your program?

Last, have you identified any special groups of donor hearts that you consider unacceptable?

DR FRANCIS ROBICSEK (Charlotte, NC): I want to congratulate Dr Sweeney and associates both for the selection of this very important subject and for the excellent presentation of this certainly vexing problem.

From their paper it is evident that in the ever-continuing quest for donor hearts we can go only in one direction: up!—up in risk and up in the age of the accepted donors! Naturally by accepting the hearts of older persons—now our upper limit is 55 years and rising—the chance that we unknowingly transplant hearts affected with coronary disease is also increasing. Because coronary cineangiography, unless the donor is in-house, is seldom feasible, we suggest the method we coined "bench-coronary cineangiography," cineangiography on the explanted donor heart just before implantation. This can be done easily in the catheterization laboratory under sterile conditions by injecting 8 to 10 mL of contrast medium directly into the coronary orifice and then washing it out with cold Ringer's solution.

When a bench coronary cineangiogram showing a normal coronary arterial tree on the right and left side is compared with the left coronary injection of coronary cineangiography before the patient died, the bench arteriogram is even more revealing than the coronary cineangiogram in the live patient.

Bench coronary arteriography is a very simple method, and we do not believe that it is in any way detrimental to the donor heart. However, this possibility is now being examined on an animal model.

DR SWEENEY: Doctor Karwande and his associates at Utah have an excellent program, which has led the way in many respects, most particularly in addressing new approaches to immunosuppression. Dr Robicsek, of course, continues to enlighten us with his intellect and with his pioneering spirit.

In answer to the Utah group's questions, we do in fact try to match high-risk hearts with high-risk recipients for a number of reasons, not the least of which being that the high-risk recipients are most likely to die first. In particular, we do match older donors with older recipients.

With regard to echocardiography, I am afraid that I cannot add much to the Utah experience. Out of 73 recipients in our HRD variable group, only 20 had echocardiograms before their cardiectomy—most of these were in the last 2 years—and of these 20 hearts, 15 were judged as normal and were used. Unfortunately, 2 of those hearts did not perform well despite their normal echocardiographic studies. It is interesting that of the 5 hearts that had abnormal echocardiographic studies, three had mitral valve prolapse and two others had wall motion abnormalities. All 5 of these hearts were used anyway, and all 5 of them performed very well. So despite the experience presented here by the Utah group, we cannot assume that echocardiography is a sensitive predictor of cardiac performance after implantation.

I guess, to sum up, we might ask ourselves if there are any donor hearts that should not be utilized. We think that the answer is still yes, but not too many. We still refuse donor hearts that are severely damaged as a result of blunt or penetrating trauma. We do not recommend using small hearts in the orthotopic position when the recipient pulmonary pressures are high. Although we had formerly avoided hearts from older donors with known coronary artery occlusive disease, we have recently performed left internal mammary artery to left anterior descending coronary artery bypass as part of the transplant procedure, and the results have been good; this may be attempted more often in the future.

Last, we would like to point out that many of the HRD hearts that are not acceptable for use in an orthotopic position could conceivably be used in a heterotopic position, functioning then as both an allograft and a human ventricular assist device, without the need to assume the entire circulatory burden. We think that standard donor criteria are logical and safe, and they have served cardiac transplant surgeons and their patients well for many years. There are occasions, however, when these criteria might be carefully extended in addressing a supply/demand mismatch. Our experience indicates that such a strategy may be appropriate for certain recipients and, when prudently applied, may result in a savings of both lives and money.

Initial Report of the Veterans Administration Preoperative Risk Assessment Study for Cardiac Surgery

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Cardiac Surgeons of the Department of Veterans Affairs

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This study was authorized by the Department of Veterans Affairs to improve the quality assurance of cardiac surgery by assessing preoperative risk factors and relating them to operative mortality. Data were received on 10,480 patients over a 2-year period. Preoperative risk variables were subjected to univariate and multivariate logistic regression analyses. Significant variables for coronary artery bypass grafting after logistic regression analysis in order of importance are previous cardiac operation, priority of operation, New York Heart Association functional class, peripheral vascular disease, age, pulmonary rales, current diuretic use, and chronic obstructive pulmonary disease. For patients undergoing valve or other cardiac operations with or without coronary artery bypass grafting, those variables found to be significant after multivariate logistic regression analysis are priority of operation; age; peripheral vascular disease; great vessel repair; all other except aortic valve replacement, mitral valve replacement, and great vessel repair; mitral valve replacement; and cardiomegaly. By identifying these current risk factors and the coefficients from the multivariate stepwise logistic regression analysis, expected mortality can be calculated. We propose that the ratio of observed to expected mortality is a better measure of quality of care than unadjusted mortality.

(Ann Thorac Surg 1990;50:12–28)

Operative mortality rates from cardiac surgical procedures are helpful in making an informed decision regarding surgical intervention for an individual patient and in assessing quality of care. In the assessment of quality of care, the actual operative mortality of an institution or cardiac surgical team can be compared with the expected operative mortality predicted from the risk characteristics of the patients undergoing surgical intervention. It has been only within the last several years that data have become available to allow quantification of operative risk from preoperative patient characteristics for both coronary artery bypass grafting [1–7] and valve replacement [8–15]. There is some information to suggest that predictors of operative risk change over time, necessitating continual monitoring [16–19]. A more recent increase in operative mortality is attributed to the increased risk of patients undergoing cardiac operations [20].

As quality assurance of medical care in cardiac surgery is being increasingly emphasized, it is imperative that more sophisticated methods of evaluating the quality of cardiac surgery be identified. In 1986, the Department of Health and Human Services Health Care Financing Administration released a list of hospitals in which mortality rates for Medicare patients allegedly exceeded predicted mortality rates for those hospitals. It was thought by The Society of Thoracic Surgeons that this was an inappropriate use of raw mortality statistics. The Society formed an ad hoc committee on risk factors for coronary artery bypass surgery, and this committee issued the following statement:

> The Society of Thoracic Surgeons remains greatly concerned about the use of raw mortality data as the sole measure to determine quality of care following coronary artery bypass surgery. Use of such data without consideration of risk factors that are predictors of hospital mortality and of other indices of quality of care is inappropriate and misleading and may adversely affect the care of the high-risk cardiac surgical patient [21].

Since 1972, the Department of Veterans Affairs (VA) has had a committee to review the quality of cardiac surgery at the approximately 50 VA Medical Centers authorized to perform this procedure (Appendix 1). This committee, known as the VA Cardiac Surgery Consultants Committee, meets twice yearly and uses operative mortality statistics submitted by the individual program directors as one measure of quality of care. It has become increasingly apparent to this committee that raw mortality statistics are an inadequate means by which to determine the quality of cardiac surgery. Indeed, the use of unadjusted operative mortality data for quality of care assessment could have an adverse ethical effect on the judgment of cardiac surgeons in that they might turn down very high risk patients whose only chance for survival would be opera-

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Table 1. Relationships of Preoperative Continuous Variables to Operative Mortality for Patients Having Coronary Artery Bypass Grafting[a]

	Survivors			Nonsurvivors			
Variable	No.	Mean	± SD	No.	Mean	± SD	p Value
Age	8,136	61.0	8.0	412	63.2	7.8	0.002
Weight (kg)	7,877	82.67	14.04	390	80.64	15.17	0.009
BSA (m^2)	7,856	1.96	0.2	389	1.94	0.18	0.007
Creatinine (μmol/L [mg/dL])	6,925	112.27 (1.27)	70.72 (0.8)	339	123.76 (1.4)	44.2 (0.5)	0.023
PaO_2 (mm Hg)	2,943	79.2	11.9	154	77.2	13.0	0.042
FEV_1	2,481	2.7	0.7	104	2.4	0.7	0.001
Height (cm)	7,859	172.5	7.75	389	171.75	7.25	0.084
$PaCO_2$	2,994	37.1	6.0	158	36.6	5.0	0.252
LV systolic pressure (mm Hg)	5,247	131.1	23.4	245	135.8	25.9	0.003
Aortic systolic pressure (mm Hg)	5,317	130.6	23.6	256	135.6	26.1	0.001
PA systolic pressure (mm Hg)	1,789	30.1	11.0	101	32.4	11.4	0.047
PA wedge pressure (mm Hg)	1,804	13.1	6.5	107	14.9	7.6	0.005
Cardiac index (L/min/m^2)	1,787	2.9	1.0	100	2.6	0.7	0.001
LV ejection fraction	6,525	0.54	0.14	337	0.50	0.15	0.001
Left main stenosis (%)	5,626	23.1	32.1	289	36.4	37.9	0.001
LAD stenosis (%)	7,424	82.7	21.0	362	86.0	19.9	0.008
Right (with PDA) stenosis (%)	7,241	82.3	27.2	361	86.9	22.8	0.006
Circumflex (with marginals) stenosis (%)	7,063	75.5	29.0	352	79.3	26.2	0.017
MD's estimate of operative mortality (%)	6,315	4.9	4.8	322	10.0	11.6	0.001
Distal disease score	4,615	1.8	1.8	231	2.3	1.9	0.001
LV contraction score	6,322	8.3	3.6	290	9.5	4.1	0.002
LVEDP (mm Hg)	5,152	15.9	7.8	240	17.0	8.6	0.051
Right atrial pressure (mm Hg)	1,629	6.5	4.1	93	6.6	4.2	0.722
LVEDV (mL)	1,633	144.3	58.5	69	148.1	64.1	0.596

[a] During the 2-year period of this study, 8,569 patients underwent coronary artery bypass grafting; 414 (4.8%) died.

BSA = body surface area; FEV_1, = forced expiratory volume in 1 second; LAD = left anterior descending coronary artery; LV = left ventricular; LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; MD = surgeon or cardiologist; PA = pulmonary artery; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension; PDA = posterior descending coronary artery; SD = standard deviation.

tive treatment. Therefore, the committee requested and was authorized by the VA to perform a risk assessment study for cardiac surgery within the Department. The purpose of this initial report is to present the significant risk factors for operative death for cardiac surgical patients during the first 2 years of data accrual.

Material and Methods

All VA cardiac surgical centers were asked to complete a single-page data form on each patient undergoing cardiac or great vessel procedures requiring cardiopulmonary bypass (Appendix 2). Clinical data included age, sex, height, weight, history of angina, chronic obstructive pulmonary disease, or associated diseases, smoking history, current medication for cardiac condition, history of previous cardiac operation, history or clinical evidence of congestive heart failure, electrocardiographic changes of ST depression or left ventricular (LV) hypertrophy, previous myocardial infarction, rest versus exertional angina, New York Heart Association functional class, creatinine value, arterial oxygen tension, arterial carbon dioxide tension, forced expiratory volume in 1 second, and operation within 7 days of angioplasty.

Also included was the estimate by the surgeon of operative death and the priority of operation, ie, elective, urgent, or emergent. The priority of operation was determined by the surgeon. Emergency procedures were usually performed on the day of catheterization. Urgent procedures were performed within several days after catheterization because further delay or discharge from the hospital was thought to be associated with increased risk. Procedures that could be scheduled at a convenient time were deemed elective.

Catheterization and angiographic data were right and left heart pressures, cardiac index, LV ejection fraction,

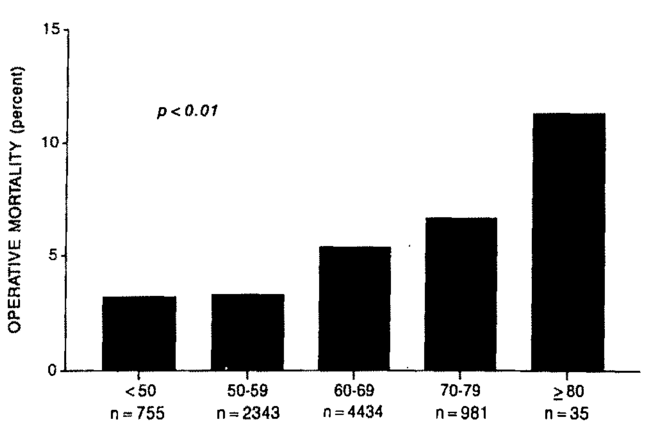

Fig 1. Effect of age on operative mortality for patients undergoing coronary artery bypass grafting. There is a marked increase in mortality for patients 80 years old or older (11.4%) versus younger patients (4.8%).

LV end-diastolic volume, location and severity of coronary stenosis, graftability of each vessel, and LV contraction score [22]. Operative data consisted of the surgical procedure including whether saphenous vein or internal mammary artery conduits were used, cross-clamp time, lowest myocardial temperature, and perioperative use of intraaortic balloon assist. Outcome data included operative death (30 days, or longer if a result of the operation) and complications.

In May and November of each year, statistical analyses were performed to assess the performance of each cardiac surgical center and to identify variables predictive of operative mortality. Identification of prognostic variables was performed separately for two groups of patients: those having coronary artery bypass grafting with and without left ventricular aneurysmectomy and those having valve operation or another cardiac surgical procedure with or without coronary artery bypass grafting. Because the latter group is heterogeneous, indicator variables identifying separately patients undergoing aortic valve replacement, mitral valve replacement, great vessel repair, and all others were added to the multivariate analyses.

The analyses were performed in two stages, a univariate screening process and a multivariate stepwise logistic regression analysis similar to that used in the VA Cooperative Study on Valvular Disease [15]. The significance of the difference between means of continuous variables and the distribution of discrete variables for operative survivors and deaths was tested with Student's t test for paired data and the χ^2 statistic, respectively. Variables having a p value of less than 0.2 were entered into the logistic regression analysis with operative death as the dependent variable.

Results

Coronary Artery Bypass Grafting

During the 24-month period from April 1, 1987, through March 31, 1989, 10,480 forms were received from 47 of the 48 hospitals performing cardiac operations. During that period, 14,475 cardiac procedures were performed. Thus, forms were received on 72% of patients having operation. There were 8,569 patients who underwent coronary artery bypass grafting, 414 (4.8%) of whom died.

The results of the univariate analyses of preoperative continuous variables are shown in Table 1, and all but five of the variables were significant ($p < 0.05$). Those with a p value of less than 0.01 are age, weight, body surface area, forced expiratory volume in 1 second, LV systolic pressure, aortic systolic pressure, mean pulmonary artery wedge pressure, cardiac index, LV ejection fraction, percent left main coronary artery stenosis, percent left anterior descending coronary artery stenosis, percent right

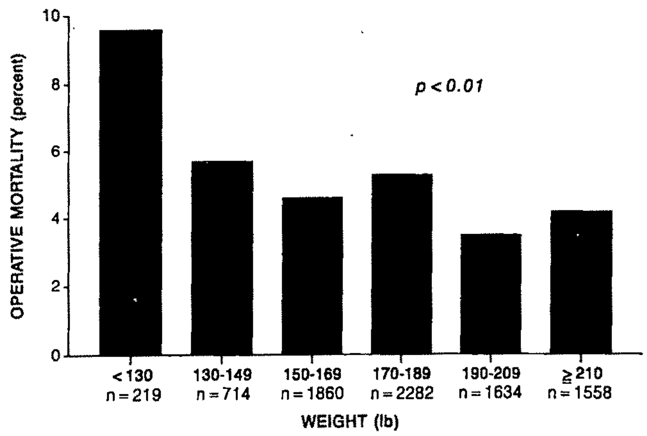

Fig 2. Effect of weight on operative mortality for patients undergoing coronary artery bypass grafting. Of interest is the fact that low weight, less than 58.5 kg (130 lb), is associated with a greater operative mortality than higher weight and obesity.

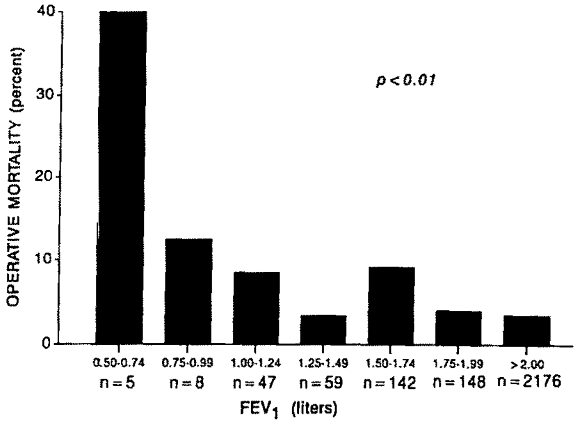

Fig 3. Effect of forced expiratory volume in 1 second (FEV_1) on operative mortality for patients undergoing coronary artery bypass grafting. Patients with an FEV_1 of less than 1.25 L/s have an operative mortality of 11.7% compared with 3.8% for those with an FEV_1 of greater than 1.25 L/s.

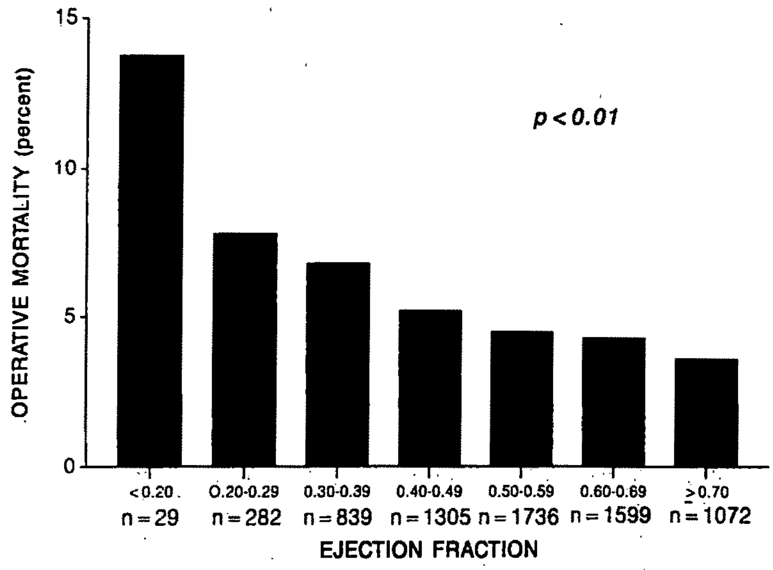

Fig 4. Effect of ejection fraction on operative mortality for patients undergoing coronary artery bypass grafting. There is a progressive increase in operative mortality as ejection fractions decrease with a 13.8% operative mortality for patients with ejection fractions less than 0.20.

coronary artery stenosis, physician's estimate of operative mortality, distal disease score, and LV contraction score.

Figures 1 through 5 display these data in a more useful clinical decision-making format by transforming some into discrete variables. Variables identifying patients with a twofold or greater increase in operative mortality are age less than 80 years (4.8% mortality) versus age equal to or greater than 80 years (11.4%) (see Fig 1), weight less than 58.5 kg (130 lb) (9.6%) versus weight equal to or greater than 58.5 kg (4.6%) (see Fig 2), forced expiratory volume in 1 second less than 1.25 L (11.7%) versus forced expiratory volume in 1 second equal to or greater than 1.25 L (3.8%) (see Fig 3), ejection fraction less than 0.20 (13.8%) versus ejection fraction equal to or greater than 0.20 (4.9%) (see Fig 4), and LV contraction score less than 15 (4.0%) versus LV contraction score equal to or greater than 15 (8.3%) (see Fig 5).

Tables 2 and 3 compare operative mortality by the presence or absence of 33 preoperative discrete variables in patients undergoing coronary artery bypass grafting. Twenty-one of these are significant predictors of operative mortality. Variables identifying patients with a twofold or more increase in operative mortality are intravenous administration of nitroglycerin preoperatively (9.4% mortality versus 3.8%), previous cardiac operation (12.5% versus 3.9%), pulmonary rales (12.0% versus 4.3%), preoperative use of an intraaortic balloon pump (15.8% versus 4.5%), New York Heart Association functional class IV versus classes I, II, or III (8.0% versus 3.3%), emergent priority of operation versus urgent or elective operations (12.6% versus 4.2%), pleural effusion (16.7% versus 5.2%), and poor general medical condition versus fair or good condition (18.8% versus 3.8%).

Figures 6 and 7 describe the development of the predictive models for patients undergoing coronary artery bypass grafting. The preoperative variables were divided into three groups: noninvasive variables reflecting chronic status, noninvasive variables reflecting acute status, and invasive variables. Because substantially more data were missing for the invasive variables, we developed two models: one based on the noninvasive variables (see Fig 6) and one based on the noninvasive plus the invasive variables (see Fig 7). Univariate analyses were performed on all preoperative variables (see Tables 1–3). Variables with a p value of less than 0.2 on univariate analysis and with less than 20% of data missing were entered into a stepwise logistic regression analysis in the groups just described. The significant ($p < 0.05$) variables from these analyses are listed in order of significance in the two rectangles in the middle of Figure 6; these significant variables were combined in a third logistic regression analysis to give the final noninvasive model consisting of (in order of significance) prior cardiac operation, priority of operation, New York Heart Association functional class, peripheral vascular disease, age, pulmonary rales;

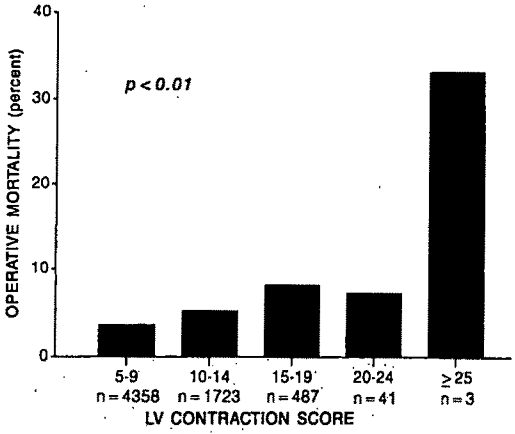

Fig 5. Effect of left ventricular (LV) contraction score on operative mortality for patients undergoing coronary artery bypass grafting. An increase in LV contraction score correlated with an increased operative mortality. Those patients with a score of 15 or more had an operative mortality of 8.3% compared with 4% for those with a score of less than 15.

Table 2. Discrete Variables Predictive of Operative Mortality For Patients Having Coronary Artery Bypass Grafting

	Variable Absent			Variable Present			
Variable	No. of Patients	Operative Deaths	%	No. of Patients	Operative Deaths	%	p Value
COPD	6,048	262	4.3	2,092	134	6.4	0.001
IV nitroglycerin preoperatively	6,546	247	3.8	1,477	139	9.4	0.001
Prior cardiac operation	7,645	299	3.9	888	111	12.5	0.001
History of CHF	7,092	304	4.3	1,176	97	8.2	0.001
Current diuretic use	5,958	234	3.9	2,063	146	7.1	0.001
Peripheral vascular disease	6,128	240	3.9	1,889	144	7.6	0.001
Cerebrovascular disease	6,850	293	4.3	1,165	91	7.8	0.001
Pulmonary rales	7,465	323	4.3	523	63	12.0	0.001
Resting ST depression	6,496	271	4.2	1,394	109	7.8	0.001
Preop IABP	8,028	363	4.5	279	44	15.8	0.001
Cardiomegaly (roentgenogram)	6,850	290	4.2	1,163	97	8.3	0.001
Old MI (> 30 days)	3,606	135	3.7	4,482	249	5.6	0.001
Recent MI (< 30 days)	6,657	284	4.3	1,499	111	7.4	0.001
Rest angina	3,500	120	3.4	4,404	267	6.1	0.001
Exertional angina	622	18	2.9	7,425	364	4.9	0.024
NYHA functional class							
I	. . .	. . .	. . .	251	2	0.8	0.001[a]
II	. . .	. . .	. . .	1,555	36	2.3	
III	. . .	. . .	. . .	3,417	132	3.9	
IV	. . .	. . .	. . .	2,523	201	8.0	
Priority of operation							
Elective	. . .	. . .	. . .	5,229	183	3.5	0.001[b]
Urgent	. . .	. . .	. . .	2,149	127	5.9	
Emergent	. . .	. . .	. . .	634	80	12.6	
No. of stenotic vessels							
0	. . .	. . .	. . .	26	0	0	0.001
1	. . .	. . .	. . .	448	10	2.2	
2	. . .	. . .	. . .	1,862	64	3.4	
3	. . .	. . .	. . .	4,443	255	5.7	
Left main stenosis ≥ 50%	4,210	163	3.9	1,705	126	7.4	0.001
Pleural effusion	2,892	150	5.2	42	7	16.7	0.006
General medical condition							
Good	. . .	. . .	. . .	1,488	38	2.6	0.001[c]
Fair	. . .	. . .	. . .	1,826	87	4.8	
Poor	. . .	. . .	. . .	319	60	18.8	

[a] Significance: $p < 0.001$ for class IV versus classes I, II, and III. [b] Significance: $p < 0.001$ for emergent priority versus urgent and elective priorities. [c] Significance: $p < 0.001$ for poor general condition versus good and fair general condition.

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; IABP = intraaortic balloon pump; IV = intravenous; MI = myocardial infarction; NYHA = New York Heart Association.

current diuretic use, and chronic obstructive pulmonary disease (COPD). Estimated mortality can be calculated from the logit equation.

The development of the model using both noninvasive and invasive variables is depicted in Figure 7. Four invasive variables were significant on univariate analysis and had less than 20% missing data; three of these entered the final invasive model: LV ejection fraction, percent right coronary artery stenosis, and percent left anterior descending coronary artery stenosis. However, none of these contributed additional prognostic information to the noninvasive model.

Valve or Other Cardiac Operation

Table 4 demonstrates the relationship of preoperative continuous variables and operative death for patients undergoing valve or other cardiac operations with or

Table 3. Discrete Variables Not Predictive of Operative Mortality for Patients Having Coronary Artery Bypass Grafting

	Variable Absent			Variable Present			
Variable	No. of Patients	Operative Deaths	%	No. of Patients	Operative Deaths	%	*p* Value
Race							
White	. . .	. . .	. . .	7,410	345	4.7	0.104
Black	. . .	. . .	. . .	552	36	6.5	
Other	. . .	. . .	. . .	334	13	3.9	
Sex							
Male	. . .	. . .	. . .	8,477	408	4.8	0.726
Female	. . .	. . .	. . .	70	4	5.7	
Diabetes	6,065	275	4.5	1,994	111	5.6	0.061
Current smoking	4,686	208	4.4	3,379	174	5.1	0.138
Ever smoked	972	36	3.7	7,003	346	4.9	0.091
Active endocarditis	8,036	389	4.8	25	0	0	0.259
Operation within 7 days of angioplasty	8,119	390	4.8	240	15	6.3	0.304
Current digitalis use	7,089	324	4.6	939	53	5.6	0.144
Current β blocker use	3,633	168	4.6	4,361	212	4.9	0.620
Current Ca^{2+} blocker use	1,495	62	4.1	6,523	318	4.9	0.232
LV hypertrophy (ECG)	6,804	316	4.6	1,030	61	5.9	0.074
Hypertension	3,345	156	4.7	4,652	232	5.0	0.507

ECG = electrocardiogram; LV = left ventricular.

without coronary artery bypass. Ten of the 24 continuous variables listed were significant ($p < 0.05$). Those with a *p* value of less than 0.01 are age, serum creatinine level, pulmonary artery systolic pressure, mean pulmonary artery wedge pressure, mean right atrial pressure, LV ejection fraction, percent left anterior descending coronary artery stenosis, percent right coronary artery stenosis, physician's estimate of mortality, and LV contraction score.

To make these data items more useful in clinical decision making, the variables just listed were transformed into discrete variables. Variables identifying patients with a twofold or more increase in operative mortality are serum creatinine level less than 132.6 μmol/L (1.5 mg/dL) (7.7%) versus serum creatinine level equal to or greater than 132.6 μmol/L (16.3%), pulmonary artery systolic pressure less than 50 mm Hg (5.5%) versus pulmonary artery systolic pressure equal to or greater than 50 mm Hg (15.4%) (Fig 8), mean pulmonary artery wedge pressure less than 13 mm Hg (6.7%) versus mean pulmonary artery wedge pressure equal to or greater than 13 mm Hg (14.2%), mean right atrial pressure less than 8 mm Hg (5.9%) versus mean right atrial pressure equal to or greater than 8 mm Hg (13.4%), LV ejection fraction less than 0.40 (14.5%) versus LV ejection fraction equal to or greater than 0.40 (6.3%) (Fig 9), and LV contraction score less than 15 (7.3%) versus LV contraction score equal to or greater than 15 (17.5%) (Fig 10).

Tables 5 and 6 show operative mortality according to 33 discrete variables; 15 of these demonstrate significant differences. Variables identifying patients with a twofold or more increase in operative mortality are active endocarditis (18.4% versus 8.6%), peripheral vascular disease (17.2% versus 7.8%), New York Heart Association functional class IV versus classes I, II, or III (16.0% versus 6.6%), emergent priority of operation versus urgent or elective operations (24.0% versus 7.5%), pleural effusion (16.3% versus 7.9%), and poor general medical condition versus fair or good condition (21.5% versus 6.4%).

Figure 11 illustrates the development of the noninvasive risk model for patients undergoing valve or other cardiac operation. The methods are the same as for patients undergoing coronary artery bypass grafting except for the use of the indicator variables: mitral valve replacement, great vessel repair, and all others except aortic valve replacement, mitral valve replacement, and great vessel repair. The significant variables for the noninvasive model in order of decreasing significance are priority of operation, age, peripheral vascular disease, great vessel repair, all other procedures (except aortic valve replacement, mitral valve replacement, and great vessel repair), mitral valve replacement, and cardiomegaly. No invasive variables with less than 20% missing data were significant by univariate analysis and therefore they were not entered into the multivariate logistic regression analysis. Estimated mortality can be calculated from the logit equation.

Comment

The Department of Veterans Affairs has a unique system of quality of care assessment or quality assurance in

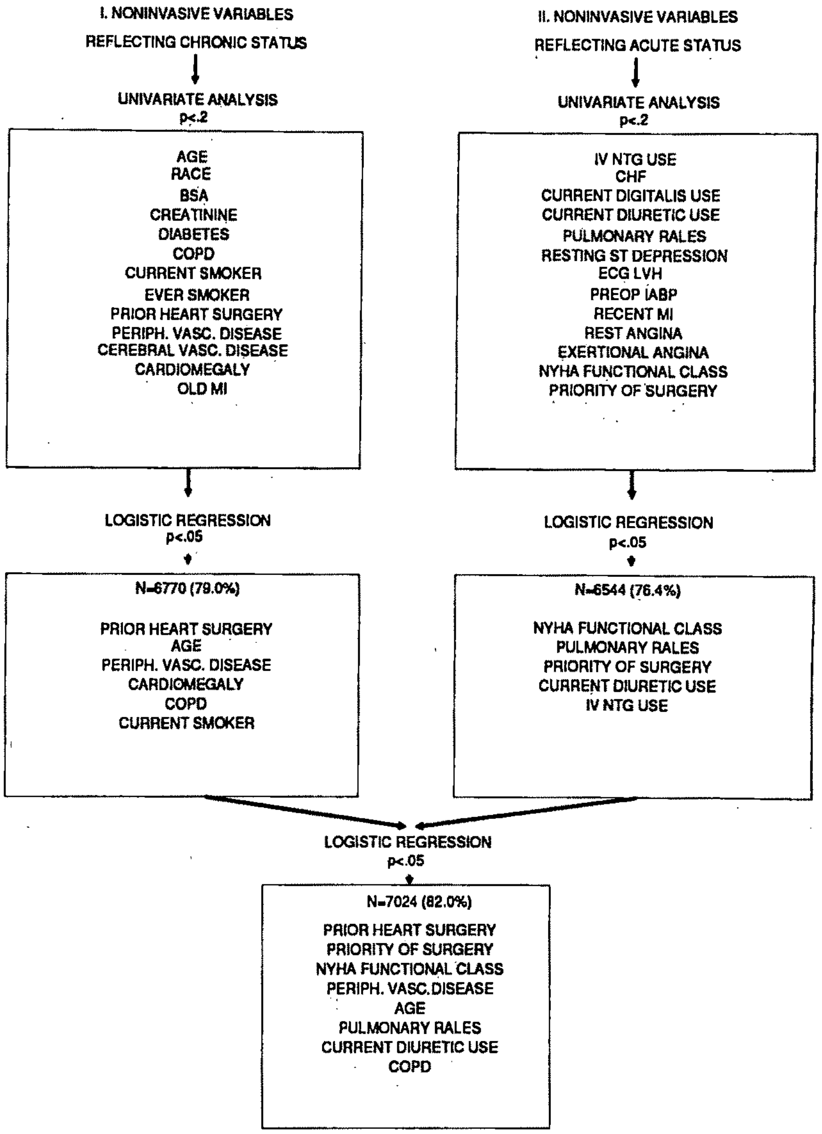

Fig 6. Results of univariate analysis and logistic regression analysis of noninvasive variables reflecting both the chronic and acute status of patients undergoing coronary artery bypass grafting (n = 8,569). The bottom box lists the variables in order of significance after the combined multivariate regression analysis. (BSA = *body surface area;* CHF = *congestive heart failure;* COPD = *chronic obstructive pulmonary disease;* ECG = *electrocardiographic;* IABP = *intraaortic balloon pump;* IV = *intravenous;* LVH = *left ventricular hypertrophy;* MI = *myocardial infarction;* NTG = *nitroglycerin;* NYHA = *New York Heart Association.)*

cardiac surgery. Since 1972, all cardiac surgical operations performed in the VA system have been reviewed by a central committee semiannually. It has become clear to the Cardiac Surgery Consultants Committee that to adequately and fairly assess the quality of cardiac surgery, the risk of the patient population and not just raw mortality data must be taken into consideration. Hanlon, in his presidential address to the American College of Surgeons [23], stated:

> Outcome and its bare essentials concerns mortality and morbidity, but the interpretation of these indicators of quality must be modified by data of how ill the patient was on entry and by other severity-of-illness measures, such as the patient's age and the presence of diseases other than the presenting reason for treatment. Neglect of severity-of-illness factors blighted the credibility of last years' federal statistics on hospital mortality, and the second public release of such data this month may suffer from a similar flaw.

Kouchoukos and colleagues [21] wrote:

> Analyses incorporating these and possibly other variables [preoperative risk variables] permit stratification and identification of subgroups of patients that are at different levels of risk for coronary artery surgery. Such analyses will also permit computation of risk models and expected operative mortality rates. Comparison of these expected or predicted operative mortality rates with observed mortality rates from different institutions will provide a more meaningful assessment of quality of care than the data provided by HCFA.

Extensive studies have been performed evaluating preoperative risk factors in patients undergoing myocardial revascularization. Hammermeister and Kennedy [1] reported in 1974 that surgical mortality was significantly increased in patients with elevated LV end-diastolic volumes, patients with ejection fractions less than 0.33, and patients with LV end-diastolic pressures greater than or equal to 18 mm Hg.

Loop and colleagues [2] in 1975 noted an increased risk for revascularization in patients with marked cardiomegaly and compensated congestive heart failure, triple-vessel coronary artery disease or obstruction of the left main coronary artery (or both), generalized impairment of LV contraction or segmental LV scar, and elevated LV

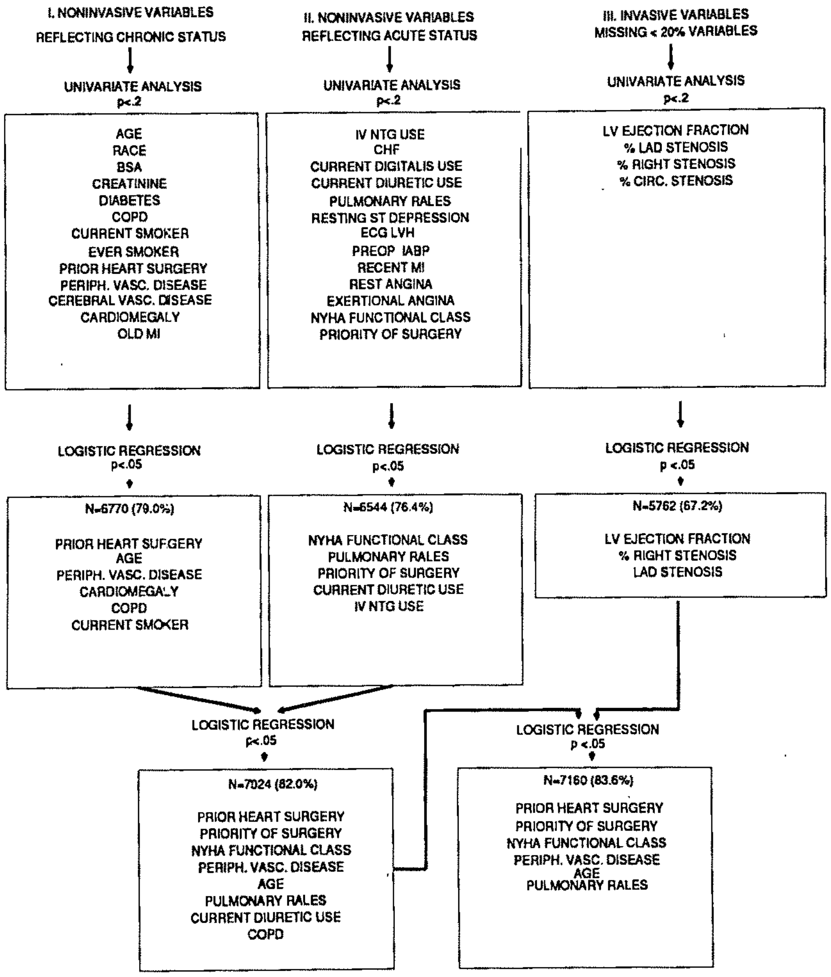

Fig 7. Results of univariate analysis and multivariate logistic regression analysis of noninvasive and invasive variables reflecting both the chronic and acute status of patients undergoing coronary artery bypass grafting (n = 8,569). The bottom right box lists the variables in order of significance after the analyses. (LAD = left anterior descending coronary artery; LV *= left ventricular; other abbreviations are the same as in Figure 5.)*

end-diastolic pressure. In their experience, the presence of congestive heart failure exerted the most influence on the probability of dying.

Kennedy and colleagues [3–5] from the Coronary Artery Surgery Study (CASS) found that mortality increased with age, female sex, presence of congestive heart failure, number of vessels involved, and left main coronary artery stenosis, particularly in patients with left dominant circulations. Operative mortality increased with impaired LV ejection fraction and with a higher LV wall motion score. In addition, urgent and emergent operations were found to have a higher mortality rate. The main factors identified by discriminant analysis of 6,176 patients in descending order of importance were age, left main coronary artery stenosis greater than 90%, female sex, LV wall motion score, LV end-diastolic pressure, and rales.

Wright and associates [7] reported that factors predictive of operative mortality in patients undergoing elective coronary artery bypass grafting were age greater than 70 years, severe (more than six stenoses) coronary artery involvement, diffuse disease, positive family history, and the number of coronary arteries bypassed.

In the late 1970s and early 1980s, there were several reports of a decrease in operative mortality in spite of increasing risk factors in coronary bypass patients. Kouchoukos and co-workers [16] reported in 1980 that in spite of operating on patients at greater risk of dying, the operative mortality had decreased for coronary artery bypass grafting from 2.7% in the early 1970s to 1.2% in the late 1970s. They attributed this improvement in survival to better perioperative management, including anesthetic and surgical techniques and intraoperative myocardial protection. In 1983, Miller and associates [17] reported a similar trend of increase in risk factors in a group operated on more recently but a decline in rates of perioperative myocardial infarction and operative mortality. Factors pertinent for the operations performed in the preceding era were no longer determinants in the latter era with the exception of emergency operation and congestive heart failure.

Cosgrove and colleagues [18] reported similar findings and noted that operative mortality decreased from 1.2% to 0.8% over a 10-year period. Of interest is that risk factors for the study period as a whole in decreasing order of significance were emergency operation, congestive heart failure, left main coronary artery disease, female sex, history of congestive heart failure, advanced age, normothermic arrest, number of grafts, poor ventricular function, and incomplete revascularization. Only advanced age, emergency operation, female sex, and congestive

Table 4. Relationships of Preoperative Continuous Variables to Operative Mortality for Patients Having Valve Operation or Other Cardiac Operation[a]

	Survivors			Nonsurvivors			
Variable	No.	Mean	± SD	No.	Mean	± SD	p Value
Age	1,733	60.4	10.8	176	63.7	9.5	0.001
Creatinine (μmol/L[mg/dL])	1,450	114.91 (1.3)	76.02 (0.86)	155	149.4 (1.69)	132.6 (1.50)	0.001
PA systolic pressure (mm Hg)	1,178	41.5	18.7	109	51.3	20.7	0.001
PA wedge pressure (mm Hg)	1,158	18.5	9.5	110	22.9	9.9	0.001
Right atrial pressure (mm Hg)	1,040	7.3	5.4	102	10.1	6.6	0.001
LV ejection fraction	1,266	0.52	0.16	110	0.47	0.16	0.001
LAD stenosis (%)	1,189	33.4	38.2	115	44.5	40.9	0.003
Right (with PDA) stenosis (%)	1,189	36.6	41.4	118	50.0	43.7	0.001
MD's estimate of operation mortality (%)	1,264	8.9	8.3	137	22.1	21.4	0.001
LV contraction score	1,206	7.7	3.5	108	9.1	4.4	0.001
Height (cm)	1,674	172.75	8	172	171.75	7.25	0.194
Weight (kg)	1,677	77.54	14.22	172	76.41	15.26	0.323
BSA (m^2)	1,673	1.9	0.18	172	1.89	0.19	0.192
PaO_2 (mm Hg)	681	78.4	13.1	70	78.7	13.5	0.843
PaCO_2 (mm Hg)	687	36.0	6.4	71	36.2	5.2	0.867
FEV$_1$	582	2.4	0.8	48	2.2	1.0	0.092
LV systolic pressure (mm Hg)	1,131	160.7	42.2	112	154.3	43.1	0.126
Aortic systolic pressure (mm Hg)	1,177	129.4	26.3	114	130.0	25.9	0.808
LVEDP (mm Hg)	1,083	19.2	9.7	107	20.7	9.2	0.129
Cardiac index (L/min/m^2)	851	2.7	1.1	79	2.6	1.3	0.474
LVEDV (mL)	317	176.1	85.0	22	173.8	68.1	0.903
Left main stenosis (%)	1,053	5.8	18.0	101	8.2	22.7	0.215
Circumflex (with marginals) stenosis (%)	1,151	30.3	39.1	106	36.9	41.4	0.096
Distal disease score	454	1.1	1.5	40	1.1	1.5	0.692

[a] During the 2-year period of this study, 1,912 patients underwent a valve operation or a cardiac procedure with or without coronary artery bypass; 176 (9.2%) died.

Abbreviations are the same as in Table 1.

heart failure persisted as predictors of operative mortality during the last time period of 1980 through 1982, and incomplete revascularization and an abnormal electrocardiogram emerged as new risk factors.

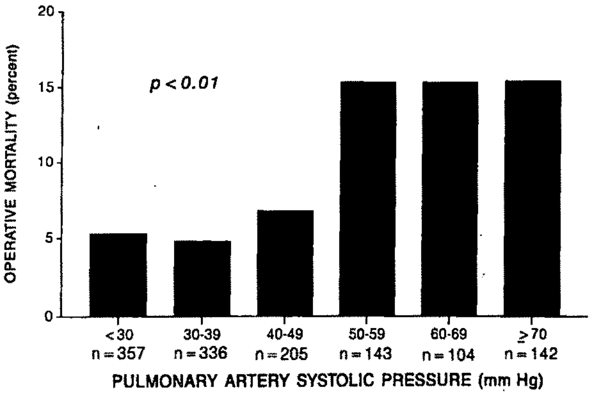

Fig 8. Effect of pulmonary artery systolic pressure on operative mortality for patients undergoing valve or other cardiac operations. There is a marked increase in operative mortality for patients with pressures of 50 mm Hg or higher.

In 1988, however, Naunheim and co-workers [20] found a significant increase in the preoperative risk factors of their patients who had had more recent operation and also an increase in the operative mortality. Preoperative risk factors that increased over a 10-year period were mean age, presence of congestive heart failure, LV dysfunction, severity of coronary artery disease, incidence of emergency operation, and incidence of associated diseases (higher frequency of diabetes, chronic lung disease, hypertension, renal dysfunction, and peripheral vascular and cerebrovascular disease). The operative mortality increased from 1% to 8% over the 10 years chiefly because of the number of patients undergoing emergency operation.

It is thus quite apparent that preoperative risk factors for the operative mortality of coronary artery bypass grafting change with time. There is little doubt, as Kouchoukos and colleagues [21] noted in their report of The Society of Thoracic Surgeons' ad hoc committee on risk factors in coronary artery bypass surgery, that major risk factors for coronary artery bypass grafting that are increasing include advanced age, reoperation, emergency

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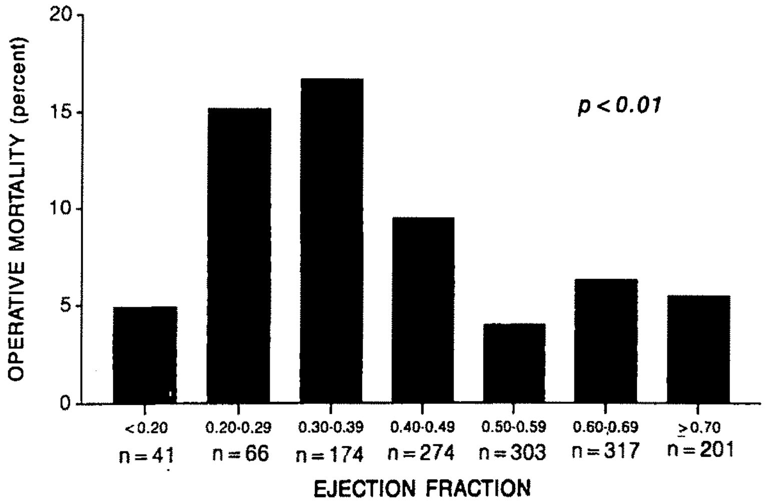


Fig 9. Effect of ejection fraction on operative mortality for patients undergoing valve or other cardiac operations. Patients with a left ventricular ejection fraction of less than 0.40 have a significantly greater operative mortality (14.5%) compared with those with higher ejection fractions (6.3%).

operation, and incidence of associated diseases. It could be that the increased risk factors are now beginning to catch up with the advanced technology in myocardial preservation, anesthesia management of patients, and preoperative and postoperative management. The VA statistics over the past 17 years substantiate this, with operative mortality for patients having multiple coronary artery bypass grafting procedures decreasing to a low of 3% in 1980 but rising as high as 4.8% in 1988.

Similar data have been obtained for patients undergoing valve operations. Scott and colleagues [8] reported in 1985 that independent determinants of operative mortality in patients undergoing aortic valve replacement were advanced New York Heart Association functional class, renal dysfunction, physiological subgroup, atrial fibrillation, and older age. In the aortic regurgitation subgroup, functional class, atrial fibrillation, and operative year were independent predictors. In the aortic stenosis subgroup, functional class, renal dysfunction, age, prosthetic valve dysfunction, and absence of angina were all significant. Scott and colleagues [9] also reported the results of a similar analysis of patients undergoing mitral valve replacement. Important predictors of mortality in these patients were New York Heart Association functional class, previous myocardial infarction, hepatic dysfunction, age, and emergency operation.

Christakis and associates [10] examined risk factors predictive of operative mortality in mitral valve operations and found the following independent risk factors in descending order of significance: New York Heart Association functional class, age, presence of coronary artery disease, presence of mitral regurgitation, and need of a tricuspid annuloplasty. Magovern and co-workers [11] reported on risk factors in patients undergoing mitral valve replacement and noted that those factors predictive of operative death were cardiogenic shock, New York Heart Association functional class IV, LV end-diastolic pressure greater than 15 mm Hg, and age greater than 60 years. Two years later, Magovern and co-workers [12] presented their aortic valve experience, which demonstrated that by multivariate analysis, the independent risk factors were emergency operation and patient age greater than 70 years. Although patients who had aortic valve replacement combined with coronary artery bypass grafting had a higher mortality, the combined operation was not an independent predictor.

Christakis and coauthors [14] examined independent predictors of operative mortality for aortic valve replacement, mitral valve replacement, and double-valve replacement. Risk factors predictive in aortic valve replacement included urgent operation, endocarditis necessitating urgent operation, previous aortic valve operation, coronary artery operation, and age. Independent risk factors for mitral valve replacement were urgent operation, endocarditis, age, coronary artery disease, and preoperative LV ejection fraction. Risk factors predictive of operative mortality for double-valve replacement were urgent operation, age, preoperative LV ejection fraction, and tricuspid valve disease.

A review of the results of our current study indicates that many of the risk factors in the studies cited are confirmed and that there is documentation of several additional risk factors. For coronary artery bypass patients, increased age was confirmed as a significant predictor of mortality. The effect of weight and body surface area was somewhat surprising in that rather than obesity

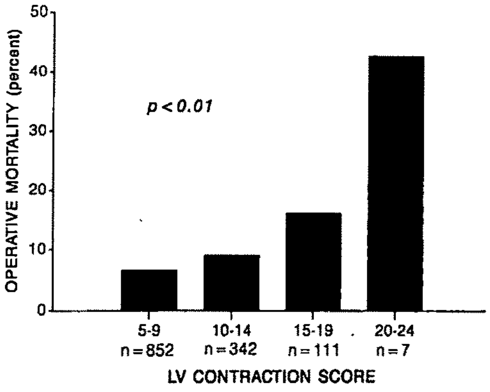


Fig 10. Effect of left ventricular (LV) contraction score on operative mortality for patients undergoing valve or other cardiac operations. Patients with an LV contraction score of 15 or higher have a much greater risk of operative death than those whose contraction score is less than 15.

Table 5. Discrete Variables Predictive of Operative Mortality For Patients Having Valve or Other Cardiac Operation

	Variable Absent			Variable Present			
Variable	No. of Patients	Operative Deaths	%	No. of Patients	Operative Deaths	%	p Value
COPD	1,263	96	7.6	535	72	13.5	0.001
Active endocarditis	1,657	143	8.6	125	23	18.4	0.001
Prior cardiac operation	1,521	124	8.2	378	50	13.2	0.002
Current digitalis use	987	78	7.9	786	87	11.1	0.023
Current diuretic use	772	57	7.4	995	107	10.8	0.015
Peripheral vascular disease	1,479	115	7.8	285	49	17.2	0.001
Pulmonary rales	1,295	107	8.3	463	59	12.7	0.005
Cardiomegaly (roentgenogram)	843	60	7.1	939	108	11.5	0.002
Recent MI (< 30 days)	1,719	156	9.1	84	13	15.5	0.049
Hypertension	1,060	82	7.7	708	86	12.1	0.002
NYHA functional class							
I	. . .	. . .	. . .	148	16	10.8	0.001[a]
II	. . .	. . .	. . .	327	23	7.0	
III	. . .	. . .	. . .	714	40	5.6	
IV	. . .	. . .	. . .	449	72	16.0	
Priority of operation							0.001[b]
Elective	. . .	. . .	. . .	1,143	63	5.5	
Urgent	. . .	. . .	. . .	398	52	13.1	
Emergent	. . .	. . .	. . .	171	41	24.0	
No. of stenotic vessels							0.005[c]
0	. . .	. . .	. . .	641	42	6.6	
1	. . .	. . .	. . .	164	19	11.6	
2	. . .	. . .	. . .	153	14	9.2	
3	. . .	. . .	. . .	178	26	14.6	
Pleural effusion	567	45	7.9	80	13	16.3	0.015
General medical condition							0.001[d]
Good	. . .	. . .	. . .	289	13	4.5	
Fair	. . .	. . .	. . .	383	30	7.8	
Poor	. . .	. . .	. . .	135	29	21.5	

[a] Significance: $p < 0.001$ for class IV versus classes I, II, and III. [b] Significance: $p < 0.001$ for emergent priority versus urgent and elective priorities. [c] Significance: $p < 0.005$ for three stenotic vessels versus none, one, and two stenotic vessels. [d] Significance: $p < 0.001$ for poor general condition versus good and fair condition.

COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; NYHA = New York Heart Association.

being associated with a higher mortality, smaller patients had an increased risk. This was also noted by Rich and associates [24] in their study of patients older than 75 years and by one [25] of the CASS studies, which demonstrated that the higher risk in female patients is the result of smaller body size. Our study, unlike previous studies, documented that the presence of COPD, as shown by hospitalization or medication usage for COPD, a decreased arterial oxygen tension, or a decreased forced expiratory volume in 1 second, was associated with a higher operative mortality. Hypertension, as measured by both LV systolic pressure and aortic systolic pressure, was noted to be a predictor of operative mortality. Ejection fraction was a strong predictor of mortality, as it has been in many studies [3–5]. Left main coronary artery stenosis was associated with increased mortality, particularly if it was equal to or greater than 70%. The LV contraction score was noted to be a significant predictor of mortality, as in CASS studies [3–5].

When the discrete variables in VA patients undergoing coronary artery bypass grafting are examined by looking simply at whether the variable was absent or present, we find that the presence of COPD increased operative mortality by 1.5 times. This has not been reported previously. The use of intravenous nitroglycerin preoperatively increased mortality. Reoperation had a profound effect on operative mortality; it increased the risk 3.2 times. A history of congestive heart failure and other indices of failure was associated with an increase in operative mortality. Of interest is the effect of both peripheral vascular and cerebrovascular disease, the former causing a 1.9-fold increase in mortality and the latter, a 1.8-fold increase in mortality. These factors have not been identified in most other studies.

Table 6. Discrete Variables Not Predictive of Operative Mortality for Patients Having Valve or Other Cardiac Operation

	Variable Absent			Variable Present			
Variable	No. of Patients	Operative Deaths	%	No. of Patients	Operative Deaths	%	p Value
Race							
White (1)	. . .	. . .	. . .	1,555	137	8.8	0.219
Black (2)	. . .	. . .	. . .	226	28	12.4	
Other (3)	. . .	. . .	. . .	81	8	9.9	
Sex							
Male (1)	. . .	. . .	. . .	1,866	173	9.3	0.637
Female (2)	. . .	. . .	. . .	42	3	7.1	
Diabetes	1,532	139	9.1	228	24	10.5	0.480
Current smoking	1,095	96	8.8	675	70	10.4	0.261
Ever smoked	325	28	8.6	1,417	135	9.5	0.611
IV nitroglycerin preoperatively	1,642	148	9.0	121	16	13.2	0.124
Operation within 7 days of angioplasty	1,835	169	9.2	13	2	15.4	0.342
History of CHF	784	60	7.7	1,048	108	10.3	0.052
Current β-blocker use	1,443	128	8.9	306	33	10.8	0.293
Current Ca^{2+} blocker use	1,251	117	9.4	499	45	9.0	0.827
Cerebrovascular disease	1,538	144	9.4	221	20	9.0	0.881
Resting ST depression	1,473	130	8.8	260	32	12.3	0.075
LV hypertrophy (ECG)	812	77	9.5	915	86	9.4	0.953
Preop IABP	1,796	162	9.0	44	8	18.2	0.058
Old MI (> 30 days)	1,395	123	8.8	379	45	11.9	0.072
Rest angina	1,384	134	9.7	328	29	8.8	0.641
Exertional angina	975	94	9.6	777	70	9.0	0.652
Left main stenosis ≥ 50%	1,069	91	8.5	85	10	11.8	0.307

CHF = congestive heart failure; ECG = electrocardiogram; IABP = intraaortic balloon pump; IV = intravenous; LV = left ventricular; MI = myocardial infarction.

The use of an intraaortic balloon pump preoperatively was associated with a 3.5-fold increase in mortality. Rest angina was associated with a 1.8-fold increase in mortality. A patient in New York Heart Association functional class IV had a 2.1-fold greater chance of dying than a patient in functional class III. A patient having an emergent operation had a 3.6-fold greater chance of dying than a patient having an elective operation, and a patient having an urgent operation was 1.7 times more likely to die than a patient having an elective operation.

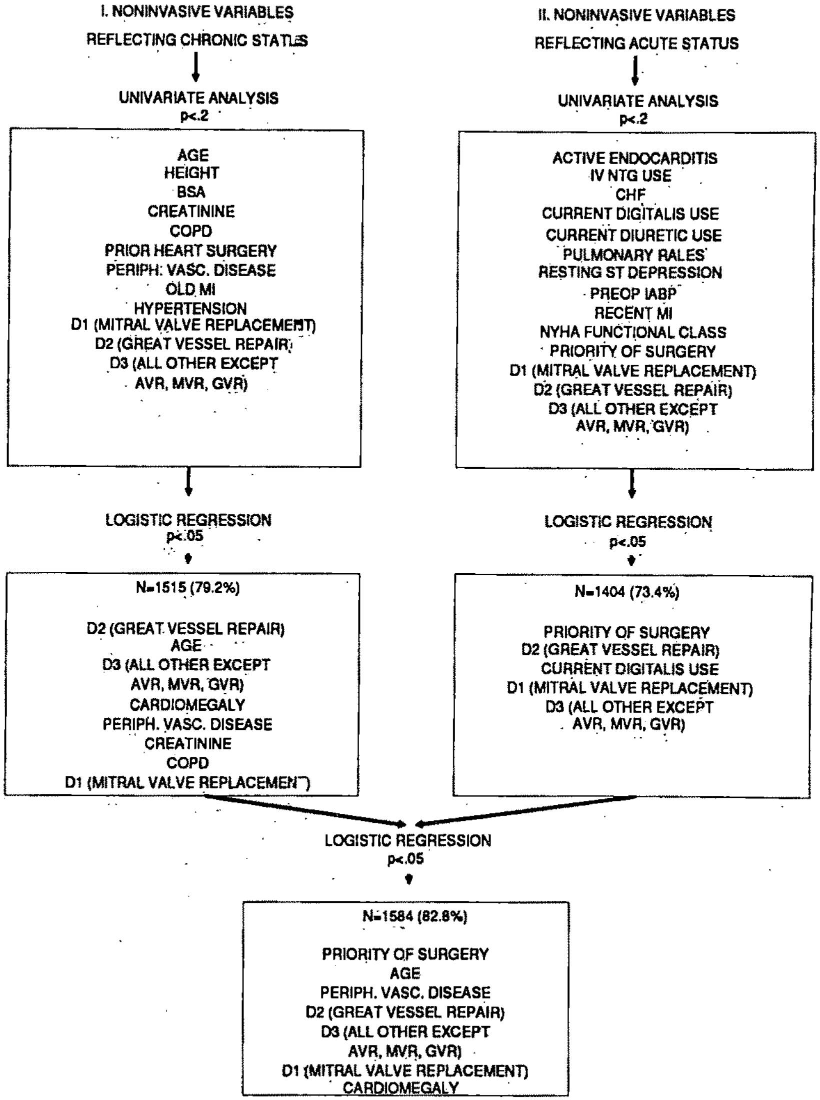
In addition, this study demonstrated the usual increase in operative mortality associated with increasing numbers of stenotic vessels and the presence of critical left main coronary artery disease. Pleural effusion had a profound 3.2-fold effect on operative mortality. The physician's impression of the patient's general medical condition demonstrated a high correlation with outcome.

Of the variables of significance in the logistic regression analysis, prior cardiac operation and priority of operation (elective versus emergent versus urgent) were the two leading prognostic indicators. This is of considerable importance at this time because of the increasing number of patients having reoperation and patients operated on for unstable angina or during acute events. Somewhat unique in this study is the documentation of peripheral vascular disease and COPD as important predictors of operative mortality. Of note is the absence of sex as a predictor of mortality. This is largely due to the very limited number of women operated on in the VA system. Diabetes was almost a significant predictor of operative mortality.

Continuous variables predictive of mortality for patients undergoing a valve or other cardiac operation with or without coronary artery bypass grafting were increased age, decreased renal function, elevated pulmonary artery systolic pressure, mean pulmonary artery wedge pressure, right atrial pressure, decreased LV ejection fraction, percent left anterior descending or right coronary artery stenosis, and decreased LV contractility as denoted by the contraction score. These risk factors substantiate other study findings.

When the findings for discrete variables for valve or other cardiac operation are reviewed, a greater risk is present for patients who have COPD, active endocarditis, prior cardiac operation, evidence of congestive heart failure, peripheral vascular disease, recent myocardial infarction, and hypertension. There is a 2.9 times greater chance of dying for those who are in functional class IV compared with those in functional class III. There is a 4.4 greater chance of dying for those who have an emergent

Figure 11. Results of univariate analysis and multivariate logistic regression analysis of noninvasive variables reflecting both the chronic and acute status of patients undergoing valve or other cardiac operations (n = 1,912). The bottom box identifies the predictors of operative mortality in order of significance after the multivariate regression analysis. (AVR = *aortic valve replacement;* GVR = *great vessel repair;* MVR = *mitral valve replacement; other abbreviations are the same as in Figure 5.)*



operation versus an elective operation, and a 2.4 times greater chance of dying for those who have an urgent versus an elective operation. There was no effect from race, and there was no difference in mortality between male and female patients; however, the proportion of nonwhite patients and female patients was small. There was some increase in operative mortality associated with the coexistence of coronary artery disease. In this study, COPD, prior cardiac operation, associated peripheral vascular disease, recent myocardial infarction, hypertension, and priority of operation were found to be strong predictors of operative mortality.

The statistical techniques used for this study were very similar to those developed for CASS [3–5] and other studies [7, 17]. The statistical study involves first a univariate analysis, which initially identifies variables thought to be either significant or marginally significant when tested singly. Second, the variables are placed into a multivariate regression analysis, which is carried out in a stepwise manner, eliminating the variable with the least significance at each step until only significant variables ($p < 0.05$) remain. By this stepwise technique, those variables that have the strongest predictive power for operative mortality are selected by eliminating those that have redundant prognostic information. This model not only selects those with the greatest predictive value, but it ranks them according to their relative influence. These can then be used in the formula to calculate the probability of a surgical death.

One shortcoming of this model is the amount of data required on the VA data form. Although this data form is only one page long, it requires the entry of angiographic data including the grading of distal coronary artery disease and the LV contraction score, which take additional time. The methodology we have used in this VA study is still in the process of being refined. Observed to expected mortality rates are being calculated for each of the participating VA hospitals and for ten private and university hospitals so that a comparison can be made between the VA database and that of the other hospitals. This technique must still be validated, and because of missing data items, the data collection must be simplified. Based on our initial 2-year gathering of risk factors, we are now in a position to eliminate many of the factors that do not have a strong predictive weight and thus simplify the data collection.

This report summarizes the initial phases of a project to use operative mortality adjusted for patient risk as a measure of quality of care in cardiac surgery. Somewhat surprisingly, we found that all of the predictive information is carried in a small group of easily obtained noninvasive variables. The next phase of this study will be to simplify data collection to improve completeness. An important subsequent step will be to identify process and structure care variables that predict outcome after patient-related risk factors have been taken into account. Thus, if deficient quality of care is identified, remedial steps and resources could be appropriately directed.

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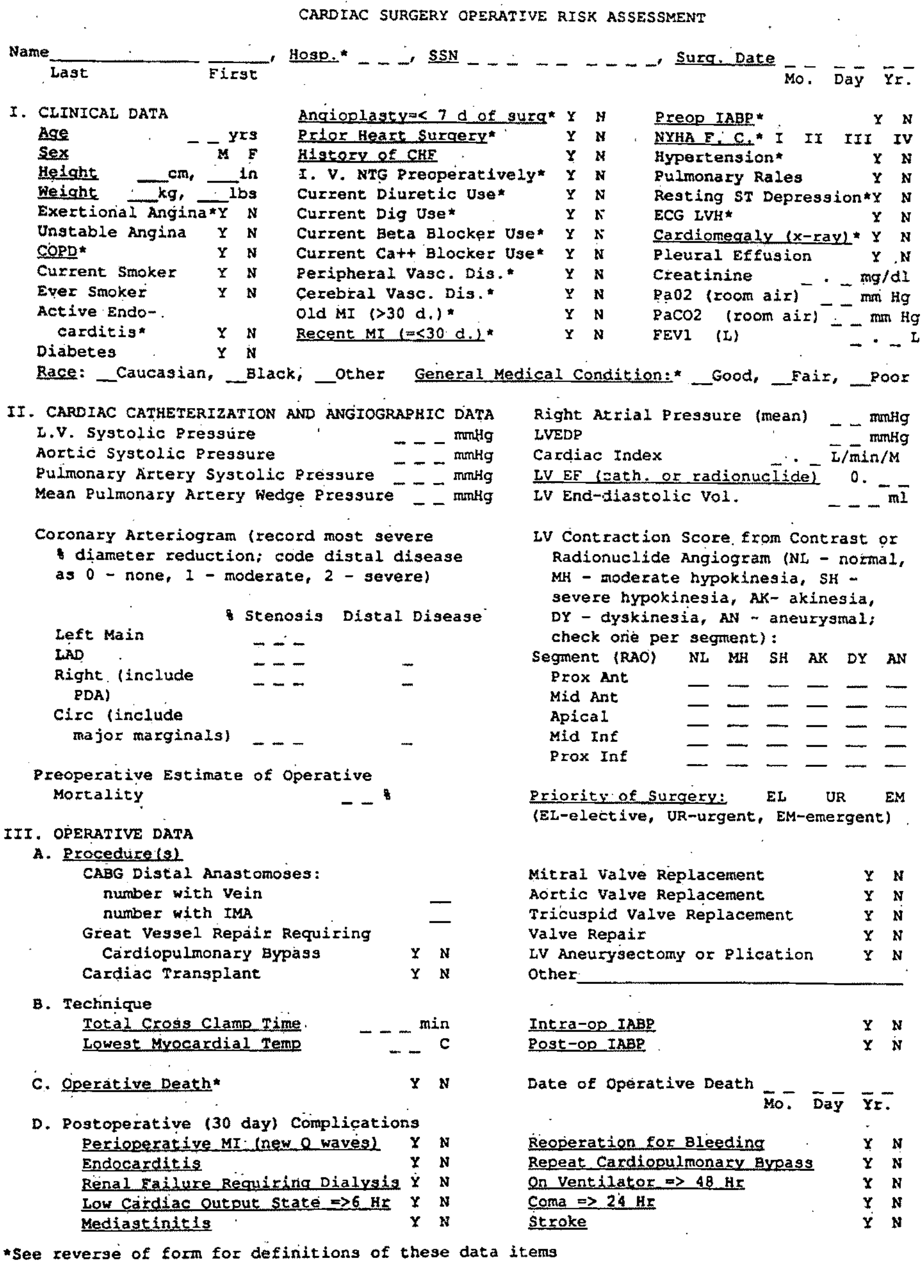
Appendix 1. Participating Physicians

Cardiac Surgery Consultants Committee members: Chair: *San Antonio, TX*: Frederick L. Grover, MD; *Asheville, NC*: Stewart M. Scott, MD; *Boston, MA*: Sidney Levitsky, MD; *Cleveland, OH*: Jay L. Ankeney, MD; *Columbia, SC*: J. O'Neal Humphries, MD; *Denver, CO*: Karl E. Hammermeister, MD; *Durham, NC*: David C. Sabiston, MD; *Los Angeles, CA*: Shahbudin H. Rahimtoola, MD; *Madison, WI*: George M. Kroncke, MD; ex officio members: *Washington, DC*: Armand A. Lefemine, MD, and Gerald O. McDonald, MD.

Those responsible for data collection at VA Hospitals participating in this study are: *Albuquerque, NM*: Stuart Pett, MD, Richard Rode, PA-C; *Ann Arbor, MI*: Mack Stirling, MD, Joyce Kerpchar, PA; *Asheville, NC*: Stewart Scott, MD, Mitch Saffie; *Atlanta, GA*: James Sink, MD, Gerard Forest, PA-C; *Augusta, GA*: Ganesh Pai, MD, Myra Metts; *Birmingham, AL*: Albert Pacifico, MD, Bill Holman, MD; *West Roxbury/Brockton, MA*: Shukri F. Khuri, MD, Sarah Orfici, PA, Rick Armenia; *Buffalo, NY*: Leon Levinsky, MD, Michelle Lewis, RN; *Charleston, SC*: Carolyn Reed, MD, Buddy Wearmouth, PA; *Chicago (West Side), IL*: Norman A. Silverman, MD, Mandya Vishwanath, MD; *Cleveland, OH*: Diana Whittlesey, MD; *Columbia, MO*: Richard A. Schmaltz, MD, Jo LaFoy, CT Nurse; *Dallas, TX*: Aaron Estrera, MD, Burlean Huff, RN; *Denver, CO*: Glen Whitman, MD, Amy Cohan, RN, MN; *Durham, NC*: Kim Lyerly, MD, Julia Smith, CT Nurse Clinician; *Gainesville, FL*: Edward Staples, MD, Gertie Walker; *Hines, IL*: Roque Pifarre, MD; *Houston, TX*: Arthur C. Beall, Jr, MD, Thomas Hurdle; *Indianapolis, IN*: Yousuf Mohamed, MD, Fran Correll, RN; *Iowa City, IA*: Douglas M. Behrendt, MD, Deb Yoder, RN, Ann Hunter; *Jackson, MS*: E. Taliaferro Warren, MD; *Kansas City, MO*: H. Daniel Lewis, MD, Wilma Payne, RN; *Lexington, KY*: Richard Floyd, MD, Patricia Martin; *Little Rock, AR*: Stephen VanDeVanter, MD, John Williams, PA; *Memphis, TN*: Charles Eastridge, MD, Betty Evans, MSN; *Miami, FL*: George M. Palatianos, MD, Lois Stockhousen; *Milwaukee, WI*: George Haasler, MD, Mary Ann T. Fabich; *Minneapolis, MN*: Herbert Ward, MD, Marge Scheftel, RN; *Nashville, TN*: Walter H. Merrill, MD; *New Orleans, LA*: Rudolph Weichert, MD, Tina Talbird; *New York, NY*: Rick Esposito, MD, Vincent Fischer, MD; *Oklahoma City, OK*: Ronald C. Elkins, MD, Joy Rodenberger; *Palo Alto, CA*: Donald Rowles, MD; *Portland, OR*: H. Storm Floten, MD, Hugh Gately, MD; *Richmond, VA*: Szabolcs Szentpetery, MD; *Salt Lake City, UT*: Shreekanth V. Karwande, MD, Sue Goldberg, RN; *San Diego, CA*: Riyad Y. Tarazi, MD, Michael P. Kaye, MD, Jennifer Bloomquist, RN; *San Juan, PR*: Manuel E. Lores, MD, Nelson Estepa, RN, CP; *Seattle, WA*: Carol Alcott; *St. Louis, MO*: Keith Naunheim, MD; *Tampa, FL*: Michael Sweeney, MD, Shelly MacIntire, Jocelyn Hall; *Tucson, AZ*: Gulshan Sethi, MD, Marty Haluza; *West Los Angeles, CA*: Davis Drinkwater, MD; *San Francisco, CA*: Edward Verrier, MD, Marc Marcotte, PA; *Madison, WI*: George Kronke, MD, K. K. Anderson; *San Antonio, TX*: Frederick L. Grover, MD, Bobbie Scallorn, RN; *Pittsburgh, PA*: Peter F. Ferson, MD, Nancy Krokosky, RN.

Appendix 2. Data Collection Form



CARDIAC SURGERY OPERATIVE RISK ASSESSMENT

Name ______________ (Last) ______ (First), Hosp.* ___, SSN ___ __ ____, Surg. Date __ (Mo.) __ (Day) __ (Yr.)

I. CLINICAL DATA

Age	___ yrs	Angioplasty=< 7 d of surg*	Y N	Preop IABP*	Y N
Sex	M F	Prior Heart Surgery*	Y N	NYHA F. C.*	I II III IV
Height	___cm, ___in	History of CHF	Y N	Hypertension*	Y N
Weight	___kg, ___lbs	I. V. NTG Preoperatively*	Y N	Pulmonary Rales	Y N
Exertional Angina*	Y N	Current Diuretic Use*	Y N	Resting ST Depression*	Y N
Unstable Angina	Y N	Current Dig Use*	Y N	ECG LVH*	Y N
COPD*	Y N	Current Beta Blocker Use*	Y N	Cardiomegaly (x-ray)*	Y N
Current Smoker	Y N	Current Ca++ Blocker Use*	Y N	Pleural Effusion	Y N
Ever Smoker	Y N	Peripheral Vasc. Dis.*	Y N	Creatinine	_ . _ mg/dl
Active Endocarditis*	Y N	Cerebral Vasc. Dis.*	Y N	Pa02 (room air)	___ mm Hg
Diabetes	Y N	Old MI (>30 d.)*	Y N	PaCO2 (room air)	___ mm Hg
		Recent MI (=<30 d.)*	Y N	FEV1 (L)	_ . _ L

Race: __Caucasian, __Black, __Other General Medical Condition:* __Good, __Fair, __Poor

II. CARDIAC CATHETERIZATION AND ANGIOGRAPHIC DATA

L.V. Systolic Pressure	___ mmHg	Right Atrial Pressure (mean)	___ mmHg
Aortic Systolic Pressure	___ mmHg	LVEDP	___ mmHg
Pulmonary Artery Systolic Pressure	___ mmHg	Cardiac Index	_ . _ L/min/M
Mean Pulmonary Artery Wedge Pressure	___ mmHg	LV EF (cath. or radionuclide)	0. ___
		LV End-diastolic Vol.	___ ml

Coronary Arteriogram (record most severe % diameter reduction; code distal disease as 0 - none, 1 - moderate, 2 - severe)

	% Stenosis	Distal Disease
Left Main	___	
LAD	___	_
Right (include PDA)	___	_
Circ (include major marginals)	___	_

LV Contraction Score from Contrast or Radionuclide Angiogram (NL - normal, MH - moderate hypokinesia, SH - severe hypokinesia, AK- akinesia, DY - dyskinesia, AN - aneurysmal; check one per segment):

Segment (RAO)	NL	MH	SH	AK	DY	AN
Prox Ant	___	___	___	___	___	___
Mid Ant	___	___	___	___	___	___
Apical	___	___	___	___	___	___
Mid Inf	___	___	___	___	___	___
Prox Inf	___	___	___	___	___	___

Preoperative Estimate of Operative Mortality ___ %

Priority of Surgery: EL UR EM
(EL-elective, UR-urgent, EM-emergent)

III. OPERATIVE DATA

A. Procedure(s)

CABG Distal Anastomoses:		Mitral Valve Replacement	Y N
number with Vein	___	Aortic Valve Replacement	Y N
number with IMA	___	Tricuspid Valve Replacement	Y N
Great Vessel Repair Requiring		Valve Repair	Y N
Cardiopulmonary Bypass	Y N	LV Aneurysectomy or Plication	Y N
Cardiac Transplant	Y N	Other________________	

B. Technique

Total Cross Clamp Time	___ min	Intra-op IABP	Y N
Lowest Myocardial Temp	___ C	Post-op IABP	Y N

C. Operative Death* Y N   Date of Operative Death __ (Mo.) __ (Day) __ (Yr.)

D. Postoperative (30 day) Complications

Perioperative MI (new Q waves)	Y N	Reoperation for Bleeding	Y N
Endocarditis	Y N	Repeat Cardiopulmonary Bypass	Y N
Renal Failure Requiring Dialysis	Y N	On Ventilator => 48 Hr	Y N
Low Cardiac Output State =>6 Hr	Y N	Coma => 24 Hr	Y N
Mediastinitis	Y N	Stroke	Y N

*See reverse of form for definitions of these data items

DISCUSSION

DR GEOFFREY M. GRAEBER (Morgantown, WV): I congratulate Dr Grover and his associates for an excellent piece of work. Their which has produced an outstanding benchmark in the assessment of realistic operative mortality for specific types of open heart operations, particularly coronary artery revascularization.

I thank them for providing me a copy of the manuscript before the meeting. To appreciate how much statistical analysis they went through, it is necessary to view the manuscript, believe me.

In performing such studies, some few individuals must be ultimately responsible for collecting, correlating, and analyzing the data. For the VA system, Dr Grover and his immediate associates certainly deserve great praise for generating this important multiinstitutional study. When I was practicing at Walter Reed Army Medical Center, Dr Fred H. Edwards, my colleague and associate, was the key individual responsible for generating similar data and analyses using Bayesian statistical theory. I am grateful to him for his suggestions, thoughts, and advice regarding Dr Grover's data. His comments were most helpful to me in preparing my discussion today.

Four points need to be emphasized:

1. Raw mortality data quite obviously can no longer be used as a predictor of outcome in myocardial revascularization or other open heart procedures. Usually we are treating patients with multiple problems that affect the outcome of any major surgical intervention. These processes must be considered in any realistic analysis of mortality.
2. Any analysis system has to be continuing and dynamic to reflect changes in patient population and improvements in therapy. Two examples of variables that emerged from this study were compromised pulmonary function and, in the paper, weight less than 58.5 kg. The former obviously correlates with increased postoperative pulmonary complications, whereas the latter probably reflects generalized poor nutritional status, which would adversely affect the outcome of any major surgical procedure.
3. Grover and associates commented in their manuscript that the format of the data sheets has to be simplified to achieve better data reporting. Variables that have insignificant predictive value need to be eliminated. Emphasis and greater priority should be placed on variables that have significantly higher predictive value in future data-collection forms. Obviously, simpler forms result in more returns and more specific data.
4. The "perfect" statistical system for predicting operative mortality really does not exist and may never exist. I agree with Dr Grover and his associates that the format will continue to evolve and will probably represent a composite of several methods. The best aspects from regression analyses used by Dr Grover and his co-workers for multiple institutions will be joined with some aspects of Bayesian theory such as we used at Walter Reed. These will be combined with certain variables of simplified format such as that recently described by Dr Parsonnet. The maturation of a "final" system will undoubtedly require some years and, indeed, may never be achieved.

I have two questions for Dr Grover. First, how did you manage standardization of subjective terms? One example is the separation of urgent from emergent.

Second, receiving data from 72% of the patients treated at nearly 50 institutions is remarkable. What methods did you use to achieve this rate?

In summary, Dr Grover and his associates have given us an outstanding body of information. I think it is essential that they continue this study throughout the coming years. I know that I myself and I am sure the rest of the members of this Society look forward to their continuing reports.

DR RALPH O. BUTZ, JR (Hines, IL): This is an impressive analysis of an impressive number of patients, but I do have some reservations about the quality of data collected.

Our hospital is required to complete and submit the data forms. We have no data collector, so the job falls on rotating junior house officers. Therefore, there is no continuity of data collectors; there is no uniform training of collectors; there is no central control of collectors; and there are no uniform procedures for data collection. If data cannot be found, the reply on the form is "unknown." This is probably due partly to a random lack of enthusiasm on the part of house officers, but it is also related to the availability of charts and other potentially disease-related information problems.

Some of the questions on this data form require subjective determination, such as the question of whether the general medical condition of the patient is good, fair, or poor. A phone call to the central data collector requesting objective criteria for this determination yielded only the information that others have answered the question without such criteria.

It is well known that surgical studies, well done and assisted by the VA Cooperative Studies Department, have shown institutions are one of the significant variables in determination of results.

I have a question concerning the potential raised here. If this survey were to be converted to an institution-evaluation project, how would you control self-serving data collection?

DR GROVER: I thank the discussants for their pertinent comments. First, Dr Graeber, thank you for your kind remarks regarding the study and the effort involved with it. It has taken an enormous effort by my many colleagues in the VA system who have contributed much data to this study, and I thank all of them. There has been very little tangible financial support for the study, so we have had to do this work mostly with existing resources within each hospital.

In answer to your question regarding urgent versus emergent operations, the priority of the operation was determined by the surgeon. Emergent operation was defined previously by CASS as an operation performed on the same day as catheterization or the event and urgent operation, as one scheduled within 1 to 6 days after catheterization or the event because further delay was deemed unwise. Elective operation included any operation that could be scheduled at a mutually convenient time.

Dr Graeber, you thought that we did well to get data on 72% of patients. We think that to make a study like this highly successful, we should have complete data on at least 80% of patients. To accomplish this, we need fiscal support for data managers at each institution and a high level of interest from all of the participating surgeons.

Dr Butz raises several points, the first of which is lack of support for data managers. I am very sympathetic to this criticism and have tried to obtain such funds. However, in this Gramm-Rudman era, such money has not been available. Most of our hospitals have been able to obtain enough local support to ensure good quality and continuity of data collection, which is current with the hospitalization of each patient, which means that chart availability is not a problem. Items for which a high enough percentage of data were not available were excluded from the risk assessment analysis. Dr Butz, your comment regarding the use of the physician's estimate of the "general medical condition" is well taken. This was included to see how close physicians can estimate the severity of a patient's overall condition and was not used to determine the risk assessment ratio because we think that for a variable, it is entirely too subjective. In answer to your question of whether we are site visiting or discontinuing VA cardiac surgery programs based on this study, we are not and will not until we have verified the methodology.

It is important for us as cardiothoracic surgeons to realize that we are in the age of consumers and consumer advocates and that they want to know what the quality of cardiac surgery is at different institutions. This is relevant not only to the VA system but to all of us. The Health Care Financing Administration has released morbidity data that do not reflect risk factors. We believe these data do not necessarily reflect the quality of surgery at a given institution, particularly at those hospitals where many high-risk patients undergo operation. The method of risk assessment we are reporting will be effective, however, only if we all agree that it is important and worthy of the investment of time required to collect high-quality data on a high percentage of patients.

Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 3, 1991. The closing date for registration is August 1, 1990.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Subvalvar Aortic Stenosis: Timing of Operation

E. Charles Douville, MD, Robert M. Sade, MD, Fred A. Crawford, Jr, MD, and
Henry B. Wiles, MD

Divisions of Cardiothoracic Surgery and Pediatric Cardiology, Medical University of South Carolina, Charleston, South Carolina

Subvalvar aortic stenosis can be associated with progressive left ventricular outflow tract obstruction, aortic insufficiency, and infective endocarditis. We reviewed the records of 36 surgical patients who underwent 39 operations for subaortic stenosis. Seventeen patients had associated congenital cardiac anomalies. One perioperative death occurred in a patient with tetralogy of Fallot. The mean preoperative left ventricular outflow tract systolic pressure gradient was 64 ± 5 mm Hg (± standard error of the mean) and decreased to 9 ± 2 mm Hg postoperatively ($p < 0.001$). Reliable preoperative and postoperative information regarding aortic valve function was available for 27 patients. Aortic insufficiency was found in 17 (63%) of those patients preoperatively. Postoperatively, insufficiency increased in 3 patients and decreased in 4; none of these changes was major. Severity of preoperative aortic insufficiency increased significantly with age ($p < 0.05$), but did not correlate with left ventricular outflow tract gradient. The information from this study and previous studies suggests that resection of subaortic stenosis is safe and effective, and operation at the time of diagnosis, regardless of left ventricular outflow tract gradient or symptomatic status, is a reasonable therapeutic alternative.

(Ann Thorac Surg 1990;50:29–34)

Congenital left ventricular outflow tract (LVOT) obstruction can be valvar (55%), subvalvar (29%), supravalvar (11%), or a combination of these (5%) [1]. Discrete subvalvar aortic stenosis can be associated with aortic insufficiency [2–4], infective endocarditis, and development of dynamic muscular obstruction [5]. Obstruction is almost always progressive [2, 3, 6–9].

In view of the progressive nature of subaortic stenosis and the high incidence of attendant complications, we recently adopted a policy of resecting all lesions shortly after diagnosis, regardless of severity of LVOT systolic pressure gradient (hereinafter referred to as LVOT gradient). To verify the rationale for this policy, we reviewed our series of patients with subaortic stenosis undergoing operation in this institution in the modern era since hypothermic potassium cardioplegia has been used and the pitfalls of this operation have been recognized.

Material and Methods

Data Collection

We reviewed the medical records of all patients undergoing operation for subaortic stenosis, excluding only those with Shone's anomaly, at the Medical University of South Carolina between July 1975 and December 1988. The record of each admission and follow-up visit was reviewed. Data collected included date of birth, date of operation, sex, associated anomalies, previous operations, and concurrent medical problems. Symptoms, chest roentgenograms, and electrocardiographic findings were also noted. Lesions were classified by surgical observation as membranous, fibromuscular, anomalous endocardial cushion tissue, or tunnel stenosis. The operation performed and early and late complications and deaths were recorded.

Echocardiograms were reviewed by one of us (H.B.W.); instantaneous left ventricular–aortic systolic pressure gradient and the presence and severity of aortic insufficiency and mitral insufficiency were noted. The degree of aortic insufficiency was classified as none (0), mild (1+), moderate (2+), or severe (3+). Echocardiography was usually performed preoperatively, postoperatively before hospital discharge, 12 months later, and at other intervals as well.

All cardiac catheterizations were performed at our institution, and the data from those studies were reviewed. Peak-to-peak left ventricular–aortic systolic pressure gradients were recorded, and the presence and severity of aortic and mitral insufficiency were noted, as were any associated cardiac abnormalities.

Surgical Techniques

Throughout the study, subaortic obstruction was resected using standard techniques of cardiopulmonary bypass under moderate hypothermia with hypothermic potassium crystalloid cardioplegia. Membranous lesions were excised by sharp and blunt dissection, often peeling them from the surface of the LVOT; membranous lesions attached to a prominent LVOT muscle (fibromuscular stenosis) were similarly excised and the muscular component treated with myotomy or myectomy. Tunnel subaortic stenosis in 1 patient was treated with a Konno-Rastan procedure [10]. Associated lesions were repaired when indicated.

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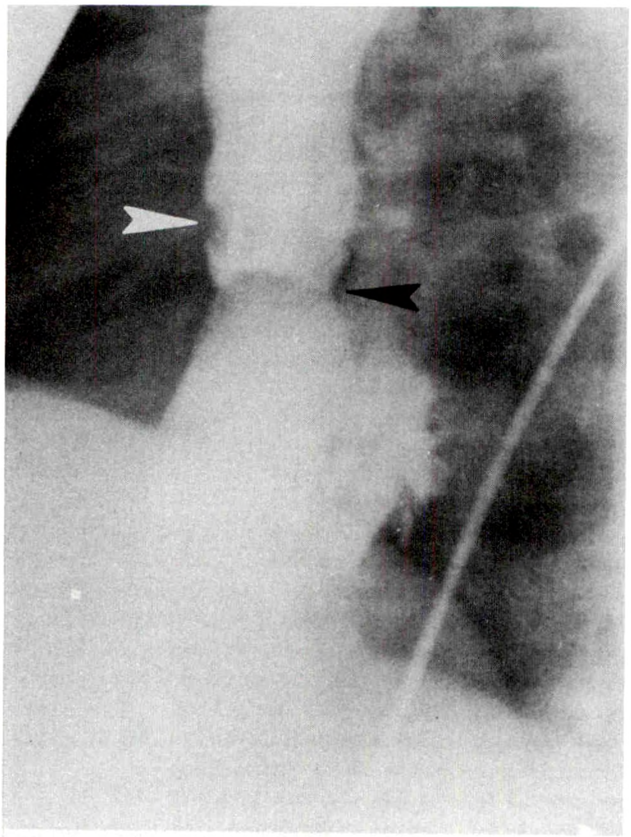

*Fig 1. Left anterior oblique projection of left ventriculogram demonstrating a subaortic membrane (*black arrowhead*) lying beneath the aortic valve (*white arrowhead*).*

Statistical Analysis

The LVOT gradients measured by echocardiography and by catheterization have been shown to correlate very highly [11, 12]; therefore we treated them interchangeably for statistical purposes. The preoperative to postoperative changes in LVOT gradient and aortic insufficiency were analyzed using the Wilcoxon signed rank test for matched pairs. The relations of aortic insufficiency to age and to LVOT gradient were analyzed using the Spearman rank correlation.

Results

Demographic Characteristics

We identified 36 patients who underwent 39 operations. There were 21 male and 15 female patients ranging in age at operation from 3 days to 52 years (mean age, 11 ± 2 years [± standard error of the mean]). None had associated noncardiac malformations. Isolated subaortic stenosis was present in 19 patients, and 17 had 26 associated congenital cardiac anomalies, including ventricular septal defect (7), ventricular septal defect with double-chambered right ventricle (2), ventricular septal defect with double-outlet right ventricle (7), atrioventricular canal (1), tetralogy of Fallot (2), atrial septal defect (1), valvar aortic stenosis (1), coarctation of the aorta (3), and patent ductus arteriosus (8).

Fourteen (39%) of the 36 patients were symptomatic with shortness of breath (6), chest pain (5), easy fatigability (4), and syncope (1). One patient was seen with endocarditis on a regurgitant aortic valve.

The morphology of subaortic stenosis at operation was membranous in 27 (69%), fibromuscular in 8 (21%), anomalous endocardial cushion tissue in 3 (8%), and tunnel stenosis in 1 (3%). The angiographic appearance of a typical subaortic membrane is shown in Figure 1 and a resected membrane, in Figure 2.

Previous repair of associated congenital cardiac anomalies had been done in 11 patients, 5 of whom had more than one associated lesion. These previous procedures included closure of a ventricular septal defect (2), repair of a ventricular septal defect with double-outlet right ventricle (1), repair of atrioventricular canal (1), correction of tetralogy of Fallot (1), aortic valvotomy (1), banding of the pulmonary artery (2), repair of aortic coarctation (3), and ligation of a patent ductus arteriosus (6).

At the time of resection of subaortic stenosis, 12 associated anomalies were corrected in 9 patients: closure of a ventricular septal defect (4) with debanding of the pulmonary artery (2) or resection of a double-chambered right ventricle (1), resection of an anomalous right ventricular muscle bundle (1), repair of tetralogy of Fallot (1), closure of an atrial septal defect (1), and ligation of a patent ductus arteriosus (2). Acquired cardiac lesions repaired concurrently with resection of subaortic stenosis in 3 patients included aortic valve replacement (2), accompanied by mitral valve replacement in 1, and pacemaker implantation for complete heart block consequent to previous repair of complete atrioventricular canal.

Five of the 36 patients had an operation for recurrence of subaortic obstruction. Two of them had had the original resection elsewhere. One was a 52-year-old man who had a subaortic membrane excised when he was 28 years of

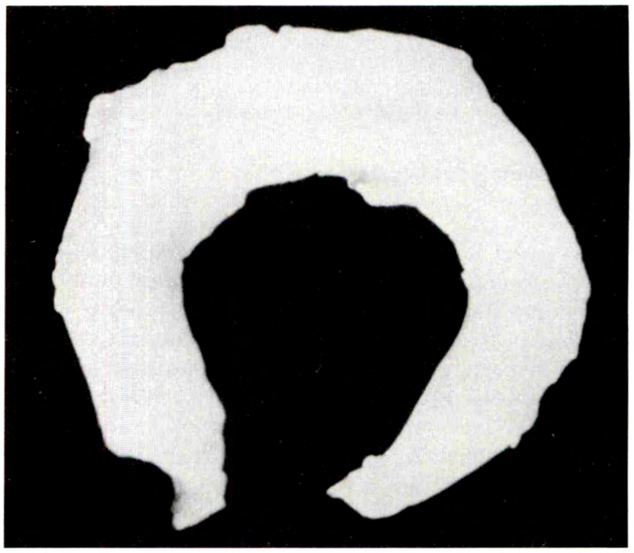

Fig 2. An entire membrane after resection. The hiatus is located at the membrane's mitral valve attachment, where the membrane was incomplete.

age and was seen with a recurrent membrane, an LVOT gradient of 20 mm Hg, and severe aortic and mitral insufficiency. The other was a 17-year-old boy who had undergone resection and myotomy for a fibromuscular lesion at the age of 9 years and subsequently was found to have a recurrent fibromuscular obstruction, which was again excised.

The 3 patients undergoing reoperation who were originally operated on at this institution included a previously reported patient with incompletely resected anomalous endocardial cushion tissue [13], a patient with membranous subaortic stenosis, and a patient originally treated for a fibromuscular lesion and later found to have tunnel stenosis, which was treated with a Konno-Rastan operation. All 3 had an LVOT gradient greater than 20 mm Hg before reoperation. Two additional patients have a postoperative LVOT gradient greater than 20 mm Hg and have not yet undergone reoperation. Thus, of the original 34 patients undergoing resection of subaortic stenosis in this institution, 5 (15%) had a residual or recurrent LVOT gradient greater than 20 mm Hg.

Deaths and Complications

There was one perioperative death. A 22-month-old boy with associated tetralogy of Fallot died of renal failure 9 days after complete repair; postmortem examination demonstrated inferior vena cava and hepatic vein thrombosis of unknown cause.

Perioperative complications included one instance of right lower lobe pneumonia and six cases of transient conduction abnormalities. The sole late complication occurred in a 16-year-old girl in whom complete heart block developed 6 months postoperatively and necessitated implantation of a permanent pacemaker.

Hemodynamic Data

The LVOT gradient decreased from 64 ± 5 mm Hg preoperatively to 9 ± 2 mm Hg postoperatively ($n = 37$) ($p < 0.001$) (Fig 3). The postoperative measurements were carried out from 3 months to 10 years after operation. Reliable measurements of both preoperative and postoperative aortic valve function were available for 27 patients; insufficiency was present in 17 (63%) of these patients preoperatively. From preoperative to postoperative measurements, aortic insufficiency increased from 0 to 1+ in 3 patients, decreased from 2+ to 0 in 2 patients, and decreased by one grade in 2 others. Aortic insufficiency was unchanged in the other 20 patients.

The severity of preoperative aortic insufficiency ($n = 29$) increased with age ($r = 0.43$; $p < 0.05$), but did not correlate with LVOT gradient ($r = 0.32$; $p < 0.20$).

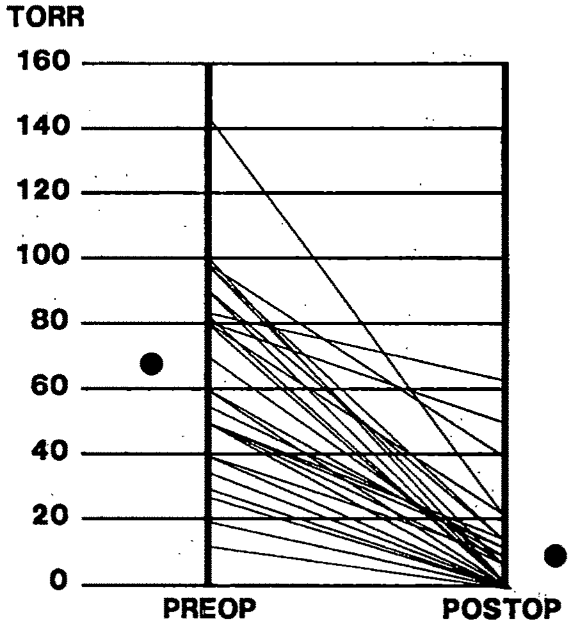

Fig 3. Change in left ventricular outflow tract gradient from preoperative measurement to postoperative measurement ($p < 0.001$). *The* closed circles *are the mean for each set of measurements.*

Comment

Chevers [14] first described subaortic stenosis in 1842, and Keith [15] later suggested that arrest of involution of the bulbus cordis was the source of the residual tissue that produced LVOT obstruction. Van Praagh and associates [16] attributed the membrane to maldevelopment of the tissues of the endocardial cushions that usually form the anterior leaflet of the mitral valve. Somerville and coworkers [5] proposed that the lesion is acquired rather than congenital because obstructive subaortic membranes occur rarely, if ever, in newborns. They suggested that abnormal flow patterns in the left ventricle result in the deposition of fibroelastic material below the aortic valve. Supporting this concept is a recent report [17] of 35 patients in whom no LVOT gradient was documented at cardiac catheterization but in whom repeat studies revealed development of a substantial gradient.

Patients with subaortic stenosis are usually asymptomatic (61% of our patients). The presence of a prominent murmur often leads to early recognition, before substantial obstruction is present. Timing of operation is therefore an important issue: delay of operation generates risk of complications related to the lesion itself, and operation subjects the patient to risks of morbidity and mortality. How can these risks best be balanced in the interest of optimal long-term results for individual patients?

There is risk in allowing the lesion to remain unresected. Aortic insufficiency in subaortic stenosis is believed to be acquired as a direct result of a high-velocity jet of blood traumatizing aortic leaflets, leading eventually to aortic insufficiency [18]. Most patients with subaortic stenosis, in fact, have abnormal aortic valves because of leaflet thickening [5].

Our study demonstrates a significant correlation between age and severity of aortic insufficiency. In this series, 17 (59%) of 29 patients with adequate studies had aortic insufficiency, which is in the same range as in other reports [3, 5, 7, 9, 11]. Most of our patients underwent operation soon after diagnosis; hence our data are insufficient to demonstrate progression of valvar incompetence in individual patients. Among our patients, however, positive correlation of severity of insufficiency with age strongly suggests progression of this acquired lesion when the underlying obstruction is not removed. The appearance of new aortic insufficiency in subaortic stenosis that has not been operated on has been documented in 6 (15%) of 40 patients 1 year to 10 years after diagnosis [9].

Two (6%) of our patients required aortic valve replacement at the time of subaortic resection because of the severity of insufficiency. Although the operative mortality rate for aortic valve replacement is very low, we [19] have previously demonstrated a high risk of late death and complications in young patients, particularly those in whom the indication for valve replacement is aortic insufficiency. Aortic insufficiency has harmful effects on myocardial ultrastructure and function that may not be reversible after valve replacement [20, 21].

During short-term (1-year) follow-up in our series, aortic insufficiency was generally unaffected by operation: it became slightly worse in 11% of patients, improved in 15%, and was unchanged in the rest. After long-term postoperative follow-up in one well-documented series of 58 patients [9], aortic insufficiency progressed during the first year in 5 (9%) and progressed in the long term in only 2 (3%), both requiring valve replacement at 15 and 24 years after operation. Thus, operative resection of subaortic stenosis probably substantially slows progression of aortic insufficiency.

Also noteworthy in the current study is the statistical demonstration that the severity of aortic insufficiency is not related to LVOT gradient, a finding supporting anecdotal observations of others [3, 8, 11]. Aortic insufficiency of any severity, when associated with subaortic stenosis, is a strong predisposing factor for the development of infective endocarditis [9].

Infective endocarditis is a serious and frequent complication of subaortic obstruction that is not treated surgically, the incidence ranging from 12% to 25% of patients [3, 7, 8], an order of magnitude higher than the incidence of endocarditis in patients with valvar aortic stenosis or ventricular septal defect. Predisposing factors are aortic insufficiency and high LVOT gradient [9]. This complication developed in only 1 (3%) of our patients preoperatively and in none postoperatively. The incidence of infective endocarditis in one large series [9] was similar preoperatively and postoperatively. All instances of postoperative infection in that series, however, were in patients with substantial residual LVOT gradients (35 to 132 mm Hg). No infection occurred postoperatively in a patient with discrete subaortic stenosis, a residual gradient less than 50 mm Hg, and no other residual anatomical lesion, criteria that fit 92% of their patients and 97% of ours. Several other series [3, 6, 8, 9] have reported an incidence of postoperative endocarditis ranging from 0% to 4%. Therefore, subaortic resection probably reduces substantially the risk of infective endocarditis.

Subaortic stenosis is a progressive disease: increasing obstruction occurred in almost all reported patients with serial preoperative studies [2, 3, 6–9]. After resection, the obstructive lesion can recur and progress, as it did in 5 (15%) of the 34 patients initially operated on in our institution.

The risks of operation are not great: only 1 (3%) of our 36 patients died, and he had a serious associated lesion. We found a low incidence of early and late complications, a finding substantiating data in previous reports [18, 22, 23]. The operation effectively relieves obstruction in most patients, as evidenced by our data and those of others [18, 22, 23].

The postoperative LVOT gradient in our patients (averaging 9 mm Hg) compares favorably with the 29 to 35 mm Hg in other series [9, 18]. Only 5 of our patients had a follow-up LVOT gradient greater than 20 mm Hg, whereas a report [18] of follow-up catheterization of 28 patients, most from an earlier era, found that all but 3 patients had an LVOT gradient greater than 20 mm Hg. This improvement could reflect better understanding in recent years of the importance of complete removal of offending tissue, and the advantage of excellent exposure provided by cold cardioplegia.

Reoperation in 3 of our patients effectively relieved the residual obstruction, and 2 others have not yet undergone reoperation. The rate of reoperation in our patients was 9% (3/34) and in previous publications ranges from 0% to 20% [2, 4–6, 18, 24, 25]. Because indications for reoperation vary widely, however, the implications of these rates are not clear. Some postoperative obstructions are undoubtedly residual, due to incomplete resection of abnormal subaortic tissue, but some are recurrent [5].

Several inferences can be drawn from our results. Aortic insufficiency caused by subaortic stenosis is progressive and can usually be prevented or stabilized by removing the stenosis. Infective endocarditis is a frequent complication of subaortic stenosis, but is rare when adequate repair of the obstruction and associated lesions has been achieved. Resection of subaortic stenosis is safe and usually effective. Because subaortic stenosis is nearly always progressive, few patients will escape eventual operation and its attendant risks.

The data cited in the discussion, our own and those of others, leave many questions unanswered, in part because follow-up of patients who have undergone the complete resection that can be achieved with contemporary surgical techniques, as in this series, is only about a decade long. Current methods of assessing surgical results, particularly echocardiography, promise reliable long-term information that is now lacking.

Although less complete than we would like, the data available from the literature and from our study seems to weigh in favor of removing the offending obstruction early, particularly if the need for reoperation can be kept to the low level we have reported. It therefore seems reasonable to resect subaortic stenosis at the time of diagnosis rather than to operate when symptoms appear or an arbitrary hemodynamic criterion is met.

The invaluable contribution to this work by our biometrician, Martha Stroud, MS, and the expert secretarial assistance of Kathryn Terry are gratefully acknowledged.

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DISCUSSION

DR JOHN W. HAMMON, JR (Nashville, TN): I congratulate Dr Douville and his co-authors on an excellent presentation of a timely subject. I was especially pleased to review their well-written manuscript before the presentation.

Their provocative hypothesis that subaortic stenosis should be resected when discovered is currently being debated in pediatric cardiac circles. I will add a caveat from our own data and ask two questions.

Dr James Stewart in our group has reviewed a similar series from Vanderbilt Hospital for the years 1972 to 1989. The two series are remarkably similar in every respect except our patients averaged 6.9 years at operation as opposed to 11 ± 2 years in the Charleston series.

During the follow-up of 1 year to 7 years (average follow-up, 38.2 months) in our series, 12 patients, or 35%, underwent repeat operation for recurrent stenosis, and the vast majority of these patients had discrete subaortic stenosis. Included in this group were 3 patients who had a discrete membrane resected for the third time.

Based on these data, we have adopted a more conservative approach to these patients and prefer to operate for symptoms, progressively increasing or severe gradients, aortic regurgitation, evidence of left ventricular dysfunction, or a combination of these.

It seems logical to us that when a discrete membrane is resected, it heals as a fibrous scar and fixes the LVOT size at that level. Because of this, it might be beneficial to delay operation in small patients if uncomplicated disease is present and if good follow-up is available.

Dr Douville, I noticed in your manuscript that you obtained echocardiographic examinations of patients before and after operation and at intervals thereafter. Did you note the development of restenosis, especially in younger patients?

Also, have you noted discrete subvalvar stenosis gradually evolving into a hypertrophic cardiomyopathy as has been reported in other series?

DR ADNAN COBANOGLU (Portland, OR): At the University Hospital in Portland, a recent review of our experience with treatment of discrete subaortic stenosis has led to a moderation of our original enthusiasm for the surgical treatment of this problem. Our series comprises 25 patients with discrete subaortic stenosis, so we did not include the more complex forms of subaortic stenosis, ie, long-tunnel stenosis. Only 1 patient in this group was less than 1 year of age. Concomitant myotomy and myectomy were added early in this series. The operative procedures performed included resection only in 10 patients, resection with myectomy or myotomy in 14 patients, and exploration of the LVOT in the 1 patient less than 1 year of age. There were no operative deaths.

Seven patients underwent reoperation at a mean interval of 4.9 years. The minimum interval was 22 months with a maximum of 8 years. The actuarial reoperation-free curve shows that although the initial results were considered excellent by us, 10 years after operation only 40% of patients had not required reoperation. The type of original operation did not correlate with late recurrence. In every reoperation, we saw an identical lesion recurring. This experience prompts us to believe that the so-called discrete subaortic ridge, ring, or stenosis is in reality not as simple as the name indicates. It is a much more complex problem.

Furthermore, we believe that the ring is not congenital but is a progressively developing acquired lesion. The disease is extremely uncommon in neonates or in infants less than 1 year of age. The fact that both the original disease and the recurrent disease as seen at operation are similar implies that the basic problem is an underlying dynamic or structural abnormality of the LVOT that produces stenosis and turbulence, and the subaortic ring develops as a response.

I have a few questions for Dr Douville. How many patients in your series were less than 1 year of age? You reported that 5 patients had recurrence, and 3 have had reoperation for recurrence. What was the actuarial recurrence rate? What were the findings at the time of reoperation? Did you observe repeat formation of the ring, ridge, or membrane similar to that seen at the first operation?

Finally, is infective endocarditis due to aortic insufficiency or is it due to continued persistent structural abnormality in the area? What is the incidence of infective endocarditis after operation for this entity?

DR ANTONIO FRANCESCO CORNO (Monza [Milano], Italy): My colleagues and I strictly follow the suggestion given in 1981 by the Boston group. Recently we reported our experience with 20 patients who underwent resection of subaortic stenosis (Chest 1989;96:325). Each patient had an LVOT gradient higher than 30 mm Hg or aortic regurgitation or both. Preoperative cardiac catheterization was not performed. There were no deaths, and no patient has had progression of aortic regurgitation.

My question for Dr Douville is, did you see any progression of the aortic regurgitation when you performed the resection in older patients?

DR DOUVILLE: Dr Hammon, we saw severe left ventricular hypertrophy in only 2 patients, both with Shone's syndrome, who were excluded from the study. Recurrent stenosis in 3 patients did not appear to be age related. The morphology in all 3 was different: 1 child had aberrant endocardial cushion tissue; 1 had fibromuscular stenosis at the initial classification that was later changed to tunnel stenosis; and 1 child had a membrane that recurred at its original site.

Dr Cobanoglu asked how many children were less than 1 year old. There was only 1 such child, a 3-day-old newborn who had aberrant endocardial cushion tissue with ventricular septal defect.

Our data were insufficient to calculate actuarial recurrence rates.

Endocarditis is probably caused by a turbulent jet across the valve. One patient was seen with endocarditis and severe aortic insufficiency. No case of endocarditis occurred postoperatively.

Three patients were found to have an increase in aortic insufficiency postoperatively, and preoperative aortic insufficiency in 4 patients disappeared postoperatively. There was no consistent effect of operation on aortic insufficiency.

Surgical Standby for Percutaneous Transluminal Coronary Angioplasty: A Survey of Patterns of Practice

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The Johns Hopkins Medical Institutions, Baltimore, Maryland

To determine patterns of surgical standby for percutaneous transluminal coronary angioplasty (PTCA), a questionnaire was mailed to 196 US institutions in which PTCA and coronary artery bypass grafting (CABG) are performed regularly. Eighty-nine responses (46%) were received and comprise this report. Of responding institutions, the mean number of hospital beds was 615. In 1987, these institutions performed a mean of 337 PTCAs and 558 open-heart surgical procedures. The rate of emergency CABG for PTCA complications (occlusion, dissection, or coronary perforation) was 4.4% ± 0.3%, whereas the rate of urgent CABG (within 24 hours) for PTCA failure was 3.7% ± 0.6%. The incidence of emergency CABG for PTCA complications was higher (5.1% ± 0.6%) among low-volume PTCA centers (less than 250 cases per year) than at high-volume centers (more than 250 cases per year) (3.7% ± 0.3%; $p < 0.05$). The most common pattern of surgical backup was to maintain an open operating room on standby (57/89, 64%), and the second most common pattern was to make the next open operating room available, allowing operating room access within 1 to 3 hours (21/89, 24%). Nearly a third of institutions (26/89, 29%) maintained a flexible backup arrangement according to PTCA risk. Routine pre-PTCA patient evaluation by surgeon and/or anesthesiologist occurred in 38% (34/89). Fees for standby services were charged by 51% of surgical teams (45/89), 39% of anesthesia teams (35/89), and 38% of operating room facilities (34/89). Thirty-seven percent of surgeons (33/89) were dissatisfied with their present standby arrangements; sources of dissatisfaction included poor communication with cardiologists about high risk or possibly inappropriate PTCA cases, waste of operating room resources, and inadequate compensation. In summary, although PTCA infrequently requires emergent surgical revascularization, many institutions still maintain an open operating room on standby. The economic burden of this support frequently is not compensated. This survey describes current practices of surgical standby for PTCA and encourages closer examination of the total cost of PTCA.

(Ann Thorac Surg 1990;50:35–9)

Surgical standby has been the standard of practice for elective percutaneous transluminal coronary angioplasty (PTCA) [1–7]. With the growth of PTCA from 24,000 procedures in 1983 to nearly 200,000 procedures in 1987 [8], the burden of providing surgical backup for PTCA has increased substantially. Despite a reduction in the rate of PTCA complications, the number of patients operated on soon after PTCA has increased [9–12]. Furthermore, PTCA patients who need emergency surgical revascularization have more extensive coronary disease and poorer ventricular function than their counterparts of 10 years ago [9, 11, 13, 14]. Providing a "safety net" for nearly one quarter of a million PTCAs a year has become more problematic for responsible surgeons.

For editorial comment, see page 3.

The generally accepted rate of PTCA complications that require emergency coronary artery bypass grafting (CABG) is low, usually less than 5% [9, 13, 15, 16]. Indeed, it has been suggested that providing omnipresent surgical standby for such a well-developed technology such as PTCA is no longer appropriate, especially in the absence of controlled studies to document the efficacy of early surgical revascularization after PTCA complications [5].

Presuming that emergency surgical intervention after PTCA preserves life and reduces the extent of myocardial infarction and that minimizing the delay between vessel injury and surgical revascularization is important, the method of surgical standby is important [4]. However, a consensus is lacking on the optimal standby arrangement. The present survey was undertaken to determine the patterns of standby commonly used by hospitals in the United States.

Material and Methods

In Fall 1988, questionnaires were mailed to 196 directors of US cardiac surgical programs in which cardiac surgery

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Presented at the Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association, Scottsdale, AZ, Nov 9–11, 1989.

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Table 1. Profile of Institutions Responding to Survey (n = 89)

Variable	Value
Mean number of hospital beds	615
Mean number of open-heart cardiac operations (1987)	558
Mean number of PTCAs (1987)	337
Rate of emergency CABG after PTCA	4.4% ± 0.3%
Rate of urgent CABG after PTCA	3.7% ± 0.6%

CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

and PTCA were performed routinely. The hospitals were chosen from a registry of the American Hospital Association [17]; all had at least 350 beds, an active cardiac surgical program, and an interventional cardiac catheterization laboratory. Responders were guaranteed confidentiality, and some responded anonymously.

Each institution was asked to provide the number of hospital beds, the number of cardiac surgical and PTCA procedures during the previous calendar year (1987), and the number of PTCA procedures resulting in emergency and urgent cardiac operations. Emergent operations were defined as those performed immediately after PTCA for complications such as coronary occlusion, dissection, or perforation. Urgent operations were defined as those performed within 24 hours after PTCA because of therapeutic failure or stable complications.

In addition, responders were asked to describe their usual mode of surgical backup by choosing from a list of options ranging from "no formal support arrangement" to "case-by-case support with an operating room and surgical team standing by." Whether pre-PTCA visits by surgeon or anesthesiologist were routine and whether fees were charged for standby services were also ascertained.

Results were compiled in a computer database and analyzed with the BMDP statistical software package (BMDP Statistical Software, Los Angeles, CA). When appropriate, complication rates were compared using Student's t test for independent data.

Results

Eighty-nine completed questionnaires were returned from 40 states, a response rate of 46%. The mean number of hospital beds among responding institutions was 615 (range, 225 to 2,000) (Table 1). These hospitals performed a mean number of 558 open-heart cardiac surgical procedures (range, 130 to 3,144) in 1987. In comparison, they performed a mean number of 337 PTCAs (range, 13 to 1,911) during the same year. Collectively, the responses describe the standby practice for 29,993 PTCA procedures in 1987.

Emergency CABG for coronary occlusion, dissection, or perforation was necessary in 4.4% ± 0.3% of PTCAs (Table 1). Urgent CABG within 24 hours for PTCA failure or for stable PTCA complications occurred in 3.7% ± 0.6%. Of all PTCA patients, 8.1% came to CABG within 24 hours.

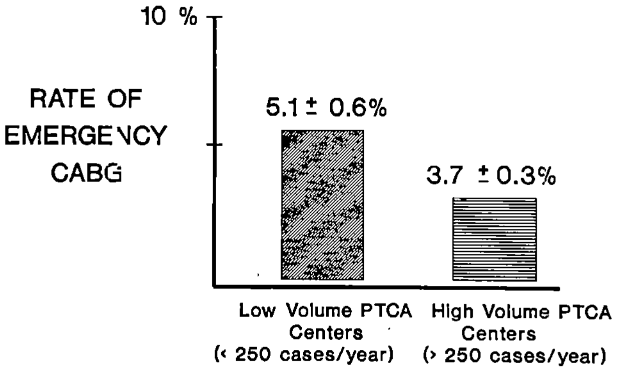

Fig 1. Effect of percutaneous transluminal coronary angioplasty (PTCA) case-load on rate of emergency coronary artery bypass grafting (CABG).

In this survey, the median number of PTCAs performed in 1987 was 250. When PTCA centers were grouped as either high-volume centers (more than 250 cases per year) or low-volume centers (less than 250 cases per year), the emergency CABG rates were significantly different ($p < 0.05$) (Fig 1). High-volume PTCA centers had a lower rate of emergency CABG (3.7% ± 0.3%) compared with low-volume PTCA centers (5.1% ± 0.6%).

The most common mode of surgical backup was to maintain an open operating room on standby (Fig 2). This was the usual method of backup in 64% of institutions. In 24% of institutions, backup was provided on a "next available room" basis. Four percent claimed to have no formal arrangements for standby, although on-site cardiac surgical facilities were a prerequisite for inclusion in the survey. Eight percent of respondents either did not describe their method of standby or elaborated several modes of standby without identifying the usual one. Nearly one third of institutions (29%) modified their usual standby arrangements for unusual or high-risk PTCA cases.

Evaluation by a surgeon, anesthesiologist, or both before PTCA occurred routinely in 38% (Fig 3). Many other surgeons reported that pre-PTCA evaluation was re-

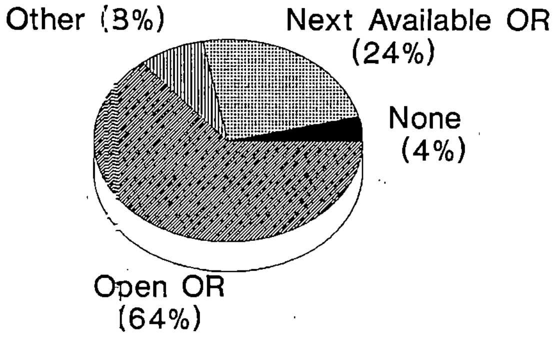

Fig 2. Modes of surgical standby for percutaneous transluminal coronary angioplasty (OR = operating room.)

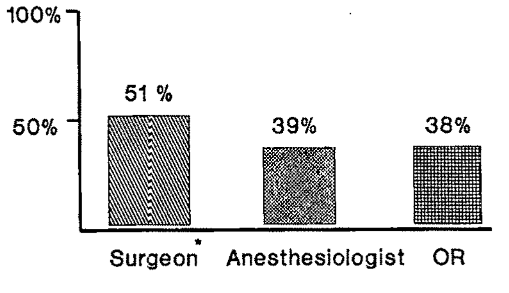

Fig 3. Frequency of billing for percutaneous transluminal coronary angioplasty (PTCA) standby services. (OR = operating room.)

served for high-risk PTCA patients or for patients with uncertain indications for PTCA.

Fees were charged for standby services by 51% of surgeons, 39% of anesthesiologists, and 38% of operating room facilities (Fig 3). The survey did not attempt to determine the usual fees for these services.

Dissatisfaction with their present standby arrangements was expressed by 37% of surgeons. Among the specific complaints noted, the most common concerned possibly inappropriate patient selection for PTCA, inadequate communication by cardiologists about high-risk patients, delay in referral of PTCAs with complications for emergent CABG, and inadequate reimbursement.

Comment

Since the inception of PTCA, a small percentage of patients undergoing the procedure have experienced complications that jeopardize life or myocardium. It has been assumed that emergency surgical revascularization is the optimum treatment for these complications [4], an assumption that seems intuitively correct, and that surgical backup is an essential part of the safe practice of PTCA.

The requirement of on-site cardiac surgical backup for PTCA has been mandated by two major task forces in the cardiology community [6, 18]. The World Health Organization and International Society and Federation of Cardiology Task Force on Coronary Angiograms and Coronary Interventions stated in its 1987 report [18] that "surgical stand-by is essential for optimal safety of the procedure." The American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty) [6] also asserted that an absolute contraindication to PTCA is absence of a formal cardiac surgical program within the institution. However, these committees have not specified what they consider to be the optimum mode of surgical standby.

That emergency surgical services are required infrequently has been well documented by the National Heart, Lung, and Blood Institute PTCA registries of 1977 to 1981 and 1985 to 1986 [9]. In the first registry, which collected data on 3,248 PTCAs performed at 105 centers over 5 years, the rate of emergency CABG was 5.8%. The second registry collected data on 2,094 PTCAs performed at 15 institutions over 2 years. The emergency CABG rate was 3.5% in the registry of 1985 to 1986 despite an increase in age, multivessel coronary disease, left ventricular dysfunction, and history of myocardial infarction in the latter PTCA cohort. The emergency CABG rate in the current survey (4.4%) was similar to those of the National Heart, Lung, and Blood Institute registries. These reports attest to technical advances and improvements in skill of PTCA practitioners, but patients who had emergency CABG after PTCA were noted to be worse surgical candidates than those from earlier years. Furthermore, although complication rates have shown a moderate decrease, the number of PTCAs performed annually has increased markedly. Thus, the total number of patients who have emergency CABG is increasing and the patients are poorer surgical candidates.

Until now, institutions have selected standby arrangements according to their own facilities and resources, taking into consideration factors of PTCA and surgical case loads, number of operating rooms, and availability of surgical, nursing, and anesthesia personnel. This has led to a wide range of standby practices. At one extreme, the catheterization laboratory and operating room coexist with little or no communication or coordination unless emergency surgical services are required. At the other extreme, all angioplasties are performed with an open operating room and a full complement of surgical, anesthesia, and nursing personnel waiting to respond. Heretofore, there have been few available data to suggest the prevalent modes of standby.

Until 1987, the practice at The Johns Hopkins Hospital was to maintain an open operating room during the morning and early afternoon for PTCA backup. No elective PTCAs were performed outside this "window." A low rate of PTCA complications with infrequent use of the operating room raised doubts that this was the optimum use of the operating room facility. In September 1987, a modified "next available room" policy was implemented, with PTCA cases scheduled between 11:00 AM and the end of the afternoon, a time that provided the shortest waiting period between a PTCA mishap and an available operating room. Discussions during this transition identified a lack of information about current patterns of standby practice elsewhere and led to the present survey.

The survey showed that a high percentage of institutions still maintained an open operating room on standby; this percentage was higher than expected as a trend toward greater use of "next available room" backup had been perceived. Twenty-four percent of survey responders used such a policy. Nearly one third of institutions had a flexible backup policy according to PTCA risk. This may be the most desirable arrangement, as the probability of surgical intervention after PTCA will vary from patient to patient. A system of risk stratification would allow better coordination of activity between the angioplasty suite and operating room.

The survey also showed that standby services frequently were not reimbursed. The rate of reimbursement was remarkably similar to that reported by Kouchoukos [16] in a survey on the economics of PTCA standby in 1985. Presumably the cost for these services was absorbed in other budgets. The cost of surgical standby has been estimated to be $1,700 for each patient, but this figure must certainly depend on the institution and its mode of standby [19]. Whatever the cost, it is probably shouldered largely by cardiac surgical patients or by all hospital patients, a situation that obscures the true cost of PTCA. These considerations are relevant to cost comparisons between PTCA and surgical therapy. Of several recent articles addressing the cost of PTCA versus the cost of CABG, none included the cost of surgical standby [20–23].

This survey was descriptive of standby practice in the US for nearly 30,000 PTCAs performed in 1987 and includes many high-volume PTCA centers. It provides information to surgeons interested in the practice patterns of their colleagues. Information on the rate of PTCA complications and failures, derived from a large collection of centers and recorded by the surgeons who treat such complications, was an additional yield of the survey. It also identified a significantly lower rate of PTCA complications among high-volume PTCA centers; although this observation appears to be predictable, the safety of PTCA in the hands of low-volume operators remained controversial in several recent reports [24–27].

Ideally, PTCA and CABG are complementary therapies in the palliative management of coronary artery disease [13]. Their respective roles have not yet been defined precisely [28]; until they are, they may occasionally be considered competitive therapies, with surgeon and cardiologist seemingly adversarial [29, 30]. Such a relationship unfortunately may interfere with the objective of optimum patient care. As PTCA and CABG find their proper respective roles, surgical backup for PTCA should be designed to provide the best possible supportive care for the PTCA patient.

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DISCUSSION

DR NORMAN J. SNOW (Cleveland, OH): Do you have any intuition from the responses or from your experience at Johns Hopkins whether the delay of next available operating room has a measurable effect on outcome? I have always been concerned that for any given patient at any given moment in the day, the next available operating room might not be available for quite some time. Do you have any sense of whether this is a problem and, if it is, what is its magnitude?

DR CAMERON: I do not have a sense about it from the survey. It appears that the shorter the delay between the complication and revascularization, the better the result. Whether that delay is short or long will depend on the institution: how many operating rooms it is maintaining, its surgical volume, and the availability of staff. Some institutions that maintain an open operating room may not have a team that can respond as quickly and as promptly as some busy centers that have an operating room available within 1 hour.

DR NICHOLAS J. SEARS (Tampa, FL): I enjoyed your paper very much, and my question echoes Dr Snow's. Did you find that the hospitals that maintained open rooms were smaller and had a lower surgical and PTCA volume than hospitals that had a next available room policy?

DR CAMERON: There was a trend toward use of next available room policy among institutions with larger cardiac surgical volumes.

DR WILLIAM D. SPOTNITZ (Charlottesville, VA): I enjoyed your paper very much. According to your classification system, how was an institution classified when it coordinated availability of an operating room with PTCAs but did not necessarily leave the operating room open? That is, if a morning CABG was finishing and the angioplasty was coordinated to be between the first and second case so that although the operating room was available and open but it really did not result in a waste of operating room time, how was that classified in your system?

DR CAMERON: They were classified as next available room.

Four Years' Experience With Fibrin Sealant in Thoracic and Cardiovascular Surgery

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A single-donor fibrin sealant system was used in 689 thoracic and cardiovascular surgical procedures over the 4-year period between April 1, 1985, and March 31, 1989. An excellent overall success rate (646/689, 94% effective) was achieved with specific applications, including reduction of leakage of air (29/33, 88% effective), blood (595/634, 94% effective), and fluid (14/14, 100% effective), as well as positioning of anatomical structures such as coronary bypass grafts (8/8, 100% effective). Application methods included use of spray bottles (477/497, 96% effective), syringes (165/186, 89% effective), and a Silastic cannula through the flexible fiber-optic bronchoscope (4/6, 67% effective). The system was used in a wide variety of cardiac, pulmonary, esophageal, and vascular procedures to seal staple lines, suture lines, anastomoses, conduits, fistulas, and raw surfaces. No complications with this single-donor system secondary to blood-borne disease have been documented. Overall infection occurred at a nominal rate (16/689, 2%). Thus, fibrin sealant has been a useful tool to control the leakage of air, blood, and fluid during a wide variety of thoracic and cardiovascular procedures and may be of benefit to other surgeons.

(Ann Thorac Surg 1990;50:40–4)

Fibrin sealant or glue is emerging as an important adjunct to surgical procedures in this country. It can be used to achieve hemostasis and can also be used to reduce air and body fluid leakage. No commercially available fibrin sealant product is presently approved for use in the United States. A variety of methods are available, however, for producing single-donor fibrinogen, which can be used in combination with bovine thrombin to produce fibrin sealant [1–5]. We have used one of these methods [5] coordinated through the blood bank since April 1, 1985. Overall hospital use per year doubled as our surgical staff became familiar with the capabilities of this method. On the thoracic and cardiovascular surgical service, this material has been particularly valuable. We report our experience using a readily available fibrin sealant system in 689 patients over a 4-year period.

Material and Methods

Fibrin Sealant Preparation

Concentrated fibrinogen is prepared routinely in the blood bank from single-donor human plasma tested for hepatitis B surface antigen and human immunodeficiency virus I antibody using a previously published method [5] easily performed in most blood banks. This technique meets the standards of the American Association of Blood Banks for blood component production and does not result in waste of valuable unstable clotting factors contained in conventional cryoprecipitate. Our method produces fibrinogen (4,003 ± 524 mg/dL) that is significantly more concentrated ($n = 10$, $p < 0.05$) as compared with American Red Cross Blood Bank cryoprecipitate containing fibrinogen (2,903 ± 1,459 mg/dL) [5]. The material can be rapidly thawed and transported to the operating room for withdrawal from a satellite pack bag (approximately 2 to 5 mL/bag) and use during operations. The blood bank maintains a permanent record of the fibrinogen used in individual patients, and records are also placed in the patient's permanent medical chart. The concentrated fibrinogen is combined with commercially available topical bovine thrombin in a ratio of 1:1. Varying concentrations of thrombin (100 to 1,000 National Institutes of Health units/mL) can be used. Higher concentrations increase the rate of sealant formation. It has not been necessary to add calcium to enhance the rate of fibrin formation in this system, and no antifibrinolytic agents were used.

Fibrin Sealant Application

A wide variety of application techniques were developed and used during the 4-year period. Initially, the concentrated fibrinogen and bovine thrombin components were placed in individual syringes with blunt-nose cannulas for simultaneous controlled local suture line application. This application method results in precise delivery of sealant to specific areas and also requires only small amounts of the individual sealant components. Thorough uniform mixing of the components is not easily achieved with this technique, however, and the technique results in a slower rate of sealant formation as well as less tensile strength.

A second method of application involved use of commercially available spray bottles [6]. This technique produces small droplets of each sealant component and

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Table 1. Fibrin Sealant Experience on the Thoracic and Cardiovascular Surgical Service, 1985–1989

Use	Success Rate (%)	No. of Cases
Overall	94	546/689
Air	88	29/33
Blood	94	595/634
Fluid	100	14/14
Position	100	8/8

results in excellent uniform mixing of up to 20 mL of each component. A rapidly forming thin layer of sealant can be applied to large surfaces with this method. This approach has been particularly valuable for dealing with bleeding from adhesions during reoperative procedures. This method may result in the use of larger volumes of sealant, however, and expose the patient to a potentially greater risk of bloodborne disease transmission.

The sealant can be applied with the aid of an absorbable cellulose or collagen sponge. After the sponge is soaked in sealant, it acts to transfer the sealant to the desired location and is a particularly effective means of arresting active bleeding. The sponge acts to tamponade bleeding while also serving as a vehicle to transport the fibrin sealant to the bleeding site.

In addition, the sealant has been applied through a Silastic cannula (Olympus Corporation of America, New Hyde Park, NY) inserted through the fiber-optic bronchoscope [7, 8]. With this method, 1 mL of fibrinogen can be followed by 1 mL of thrombin and application can occur in any segment of the bronchial tree accessible to the flexible bronchoscope. This procedure has been valuable in controlling small (<4 mm) bronchopleural fistulas.

Fibrin Sealant Effectiveness

All surgeons using fibrin sealant were asked to complete a data sheet after using the material. The operative procedure and method of application were documented, and the surgeons' subjective assessments of sealant effectiveness were recorded. Criteria for successful use of the sealant required that the surgeon judge the sealant to have been effective and that the patient not require reoperative exploration for inadequate hemostasis or for persistent air or fluid leak. Patient data were maintained in a personal computer database manager for later evaluation. This report summarizes our 4-year thoracic and cardiovascular service experience based on this database. Infectious complications were evaluated by correlating a hospital-wide database for all types of infections with the fibrin sealant database from April 1, 1985, through March 31, 1989.

Table 2. Methods of Fibrin Sealant Application

Method	Success Rate (%)	No. of Cases
Spray	96	477/497
Syringe	89	165/186
Bronchoscope	67	4/6

Table 3. Fibrin Sealant Applications During Thoracic and Cardiovascular Operations

Application	Success Rate (%)	No. of Cases
Pulmonary staples	94	17/18
Bronchial anastomoses or stump	88	7/8
Bronchopleural fistulas (bronchoscope)	60	3/5
Mediastinal bleeding	94	186/197
Coronary anastomoses	89	51/57
Conduits and suture lines	94	331/351
Esophagus	100	11/11
Other	95	40/42

Results

Fibrin sealant use on the thoracic and cardiovascular surgery service at the University of Virginia Health Sciences Center was evaluated for a 4-year period. Six hundred eighty-nine procedures were performed using fibrin sealant, with an overall success rate of 94% (646/689). Procedures included 177 coronary artery bypass graft operations, 121 valve replacements, 49 reoperation coronary artery bypass or reoperation valve replacements, 34 combined coronary bypass and valve replacements, 32 pulmonary resections, 35 thoracic aortic aneurysm or dissection repairs, 88 congenital cardiac operations, 39 abdominal aorta procedures, and 114 miscellaneous operations including esophagectomies, mediastinal reexplorations, and chest wall procedures. The material was used to control leakage of air, blood, and body fluids with excellent success rates (Table 1). It was also highly effective in positioning bypass grafts. A variety of application methods were used, including spray application as an aerosol, syringe application as a liquid, and application through a cannula placed into a flexible fiber-optic bronchoscope (Table 2). The spray method of application had the highest overall success rate (477/497, 96% effective).

Specific uses of the sealant system (Table 3) included reduction of bleeding from diffuse areas of the mediastinum, specific sites at coronary artery bypass graft anastomoses, long suture lines, and the surface of synthetic conduits. The technique was used to control air leaks from pulmonary staple lines, bronchial anastomoses, and bronchopleural fistulas. Fibrin sealant was also used to seal esophagogastric anastomoses to reduce the theoretical risk of postoperative leakage. Success rates varied between a low of 60% (3/5) for bronchopleural fistulas and a high of 100% (11/11) for esophageal anastomoses. The system was also useful in a number of other applications, including alignment of bypass grafts, sealing of chylous leakage, and reduction of potential bleeding from cardiac monitoring catheter insertion sites and of raw surface bleeding from the liver, lung, and chest wall.

Table 4. Fibrin Sealant Experience on the Thoracic and Cardiovascular Surgical Service, 1985–1989

Infectious Complication	%	No. of Cases
Overall	2.3	16/689
Superficial infection	1.4	10/689
Major infection	0.7	5/689
Pneumonia	0.1	1/689

Review of blood bank and epidemiological records showed no evidence of bloodborne disease transmission using the sealant system. The overall infection rate was nominal (16/689, 2.3%) (Table 4). Major infection requiring operative wound drainage or wound debridement occurred in 0.7% (5/689). No other sealant-related complications were noted.

Comment

Fibrin sealant or glue is an established surgical material in Europe and Canada where a commercially manufactured system is available. This product is not available in the United States because of the potential risk of bloodborne disease transmission by the fibrinogen obtained for the manufactured product from pooled human plasma. The effectiveness of the system, however, is well known, and a large body of literature emphasizes its usefulness [9–12]. With the increasing popularity of single-donor methods for obtaining concentrated fibrinogen [1–5], surgeons in this country have been gaining more clinical experience in the use of this modality [2, 13, 14].

We reviewed the use of fibrin sealant in 689 patients undergoing thoracic and cardiovascular surgical procedures over a 4-year period. During this time, the capacity to use this method has improved with experience. New methods of application [6, 7] and indications for use in general [14] as well as in thoracic and cardiovascular surgery have evolved. The support of our blood bank has been invaluable and has enabled us to use a highly concentrated and readily available form of fibrinogen with a decreased risk of bloodborne disease transmission [5].

Advantages

This study documents the successful use of fibrin sealant in a wide variety of thoracic and cardiovascular operative procedures. Mediastinal bleeding during cardiac operations is a potentially serious complication, and spray application of this system to patients with apparently excessive nonsuturable bleeding at the end of an operation reduces postoperative bleeding [13]. This effect is particularly notable during cardiac reoperation when bleeding from adhesions may be clinically significant. When fibrin glue was used in reoperation valve or coronary artery bypass graft operations, only one reexploration for bleeding was needed in 49 cases. Arterial bleeding from coronary artery anastomoses is not always controllable using this method, and fibrin sealant is never a substitute for excellent surgical technique. It will not stop arterial bleeding requiring a suture for hemostasis. When used to seal conduits, the system is particularly valuable. It avoids the necessity of choosing a graft early in a procedure. It also eliminates the need to preclot a graft with nonheparinized blood and reduces the time delay required for baking an albumin-soaked graft. In addition, the gelatinous sealant tends to reseal needle holes in the graft and prevent bleeding at suture holes. The agent can be added to long, inaccessible suture lines to reduce the risk of blood loss and is effective in congenital cardiac operations.

In pulmonary resections, fibrin sealant is useful in reducing blood and air leak from lung surfaces and bronchial anastomoses. Application of fibrin sealant to pulmonary staple lines also appeared effective. Small bronchopleural fistulas can be controlled without major operative procedures when this method is used [7, 8] in combination with the flexible bronchoscope. This may reduce morbidity and hospital costs substantially.

The system has been used to reinforce stapled gastroesophageal anastomoses, and there were no postoperative leaks in the 11 patients in whom it was used. These advantages are all potential and unproven, however, as we did not conduct any controlled prospective study confirming the capabilities of fibrin glue.

The benefits of our own technique include its easy availability from the blood bank and its reduced risk of bloodborne disease transmission [5]. It can reduce exposure to platelets, fresh frozen plasma, blood, and other products [13] when used to enhance hemostasis.

Disadvantages

This study itself was not randomized or prospective and therefore provides only historical information suggesting the usefulness of fibrin sealant, which was used only with a specific surgical indication. The method was not used in a routine prophylactic way because of the risk of bloodborne disease transmission. The surgeon using fibrin sealant must thus weigh the risks, benefits, and alternatives to its use in each individual case.

The syringe method useful for sealing suture lines and the bronchoscopic method useful for sealing bronchopleural fistulas require small amounts of fibrinogen and thrombin. The spray method useful for applying sealant to large surface areas can easily result in use of larger volumes of fibrinogen, however, which may in itself increase blood-product exposure to the patient.

Fibrin sealant is a potential growth media for bacteria and should not be used in situations in which infection is very likely to occur. In this study, use of fibrin sealant resulted in a nominal overall infection rate of 2%.

This agent is a potential antigenic stimulant and tissue reaction theoretically can be induced by its use, which theoretically can result in an inflammatory response or fibrosis. Recent work in an animal model using sealant without antifibrinolytic agents demonstrated no evidence of clinically significant inflammatory response or fibrosis with this particular system [15].

Summary

In summary, this historical study shows that a fibrin sealant system has been a useful agent in reducing leakage of air, blood, and other fluids in a wide variety of operations during 4 years of thoracic and cardiovascular surgery. Complications have not been clinically significant. The system should be used only with specific indications because the risk of bloodborne disease transmission, however minimal, does exist.

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DISCUSSION

DR THOMAS A. ORSZULAK (Rochester, MN): We are also using fibrin sealant, and I would like to ask your comments about a technique that one of my colleagues has used, more so for congenital patients, by which one of the parents is the single donor, which in the minds of my colleagues totally eliminates the risks of acquired immunodeficiency syndrome and hepatitis. For elective operations in adults, if time allows, patients can donate their own.

DR MATTHEW: I agree. We have a system by which patients can donate their own blood before operation for manufacture of fibrin sealant. But as you know, this is not a blood-type–specific product, so it certainly could be obtained from the blood of a parent or other family member. That is a very good idea, and I think we may even consider exploring it.

DR JOHN W. HAMMON, JR (Nashville, TN): We have had some experience using a fibrin sealant produced with cryoprecipitate and thrombin, so we may well be talking about apples and oranges. We have had some concerns about using the sealant in congenital heart surgery in certain patients, especially with anastomoses around the pulmonary arteries, ie, in a patient who has truncus arteriosus or perhaps arterial switch procedures. The creamy, white pannus that is produced by the use of fibrin sealant was remarkably similar in appearance several months or years later when these patients were reoperated on for various problems, and it produced quite a thick scar which we theorized was due to use of this material. Therefore, we have not used it with as much gusto in this type of patient. I wished to offer this caveat and ask whether you had any comment about it.

DR MATTHEW: Well, it is a two-part question. I will give a two-part answer. First, we are not talking about apples and oranges. The product that is made from cryoprecipitate also uses fibrinogen. In a paper we published in the *American Surgeon* in August 1987, we reported that the UVA preparation has a significantly greater concentration of fibrinogen than does the ordinary cryoprecipitate. It is greater by a magnitude of approximately two. Therefore, we believe that a lesser amount can be used and still produce a more effective fibrin sealant with the higher concentration. Second, the cryoprecipitate has unstable clotting factors that might better be used for other purposes and are not necessary for the manufacture of fibrin sealant. With regard to cost, therefore, it would be better to use the UVA method than to waste valuable cryoprecipitate.

To determine how long the fibrin glue lasts, we have performed some studies in calves. Recently, I also performed some studies in rats for the same reason. The glue is almost gone after 24 hours. We find that it sets up the matrix for healing and, in various cases, for hemostasis; in the case of bronchopleural fistulas, it allows the lung to reexpand. After about 24 hours, however, it is gone, and the body's normal function then takes over for the healing process. Therefore, I would be very surprised if the scar you found was related to the fibrin glue. In the study we preformed with chest tube drainage in calves, we found a significant decrease in chest tube drainage after operation. At postmortem evaluation of the epicardial surface, our pathologist, using special stains, could not find any evidence of fibrinogen or any extra inflammation.

DR KAMAL A. MANSOUR (Atlanta, GA): I do not want to let the principle of esophageal anastomosis be destroyed. I think it makes a lot of sense to use your sealant for bronchial leak, pulmonary leak, or blood leak. But for gastroesophageal anastomosis, everything depends on tension on the suture line, vascular blood supply, and precise surgical technique. Covering the anastomosis with a sealant while the tissues are sloughing underneath makes no sense whatsoever. I think you were lucky in that nothing bad happened, because nothing bad would have happened if you used nothing at all. This is a very serious point, and you are really attacking a very well-established principle. I disagree totally with using fibrin sealant for gastroesophageal anastomosis.

DR BENDER (President): I think Dr Mansour makes a good point. I think it is very difficult to know what success rate means in your data. The bleeding stopped, but it generally does anyway, and I think it is a difficult thing to measure.

DR MATTHEW: I agree completely that fibrin glue is not a substitute for excellent surgical technique, and certainly the surgeons at the University of Virginia are very excellent and have very good results. Therefore, they may have had no leak without the use of glue. Nevertheless, there is no reason not to make your best effort with fibrin glue as a sealant. I do not think that it harms the anastomosis, if that is the implication. If you have good surgical technique, there is no reason why you cannot use fibrin glue as an adjunct. It is not going to decrease your ability to perform a good operation.

DR WILLIAM D. SPOTNITZ (Charlottesville, VA): With regard to the issue of autologous donation of fibrinogen or directed donor sources for fibrinogen, I believe it is important to realize that blood banks are very concerned about the issues of the origin of the fibrinogen and how it is going to be donated: whether it is from cryoprecipitate or other sources. I think we should all remember that the best source clearly is autologous fibrinogen. We do have a system such as that established at the University of Virginia and try to use it preferentially.

I was concerned, however, about the issue of relatives and friends donating blood products. I think we should all remember a principle considered important by the head of the blood bank at the University of Virginia. Certainly family members who are asked to donate for a patient are not going to be able to admit objectively that they may have had bloodborne disease exposure. Therefore, I am not convinced that the family's donations are necessarily reliable blood products. I believe it is important to remember that the best solution is autologous fibrinogen.

DR FRED H. EDWARDS (Washington, DC): Do you have problems with autotransfusion after you use fibrin glue for your aortic or cardiac cases?

DR MEREDITH L. SCOTT (Orlando, FL): Is there a quantitative difference in your concentrated fibrinogen versus the cryoprecipitate that we and other doctors use? In other words, clinically, does the concentrated fibrinogen clot better than the cryoprecipitate?

DR MILTON V. DAVIS (Kaufman, TX): Jim Murphy from Oteen, who, along with Hawley Seiler and DeWitt Daughtry, started this organization, wrote extensively on bronchopleural fistula. He was probably about the only identifiable man in his era who was telling the truth, and Murphy had a Murphyism that stated: "All bronchial closures leak. It's just a matter of degree." I think he was probably right to some extent, because we have all learned to cover stumps, and the glue may have an application in such cases. It is wonderful to hear this kind of presentation and this kind of discussion. Regardless of how much some people tear it apart, the glue must have some usefulness.

DR MATTHEW: The answer to the question about autotransfusion is no. It has been postulated that the glue might clog chest tube drainage and interfere with the use of autotransfusion, but we have not had that problem and we use autotransfusion frequently. In terms of a quantitative difference between cryoprecipitate fibrinogen levels and our UVA blood bank method, there is a difference, and I refer you to the article that I mentioned. We demonstrated a statistically significant difference between the concentration of the two methods.

Esophageal Perforation: A Therapeutic Challenge

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The records of 64 patients with esophageal perforation treated since 1958 were reviewed. There were 19 cervical perforations, 44 thoracic perforations, and one abdominal perforation. Thirty-one perforations (48%) were due to injury from intraluminal causes. Twenty (31%) resulted from extraluminal causes: penetrating wounds, 11; blunt trauma, 3; and paraesophageal operations, 6. Eleven (17%) were spontaneous perforations, and two (3%) were caused by perforation of an esophageal malignancy. Ten (91%) of 11 patients with cervical perforations treated less than 24 hours after injury survived compared with 6 (75%) of 8 patients treated more than 24 hours after injury; hence 16 (84%) of the 19 patients in the cervical group survived. In the thoracic group, 19 patients were treated within 24 hours with 16 survivors (84%) compared with 25 patients treated beyond 24 hours with 12 survivors (48%); hence 28 (64%) of the 44 patients in the thoracic group survived. The patient with an abdominal perforation survived. Thirty patients underwent primary suture closure of the perforation, and 25 (83%) lived. Seventeen patients had drainage, and 10 (59%) lived. Total esophagectomy was performed in 9 patients, 7 (78%) of whom survived. Exclusion-diversion procedures were performed in 5 patients, and 1 (20%) survived.

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Esophageal perforations continue to carry a serious prognosis because of the associated high rate of morbidity and mortality [1]. The unique anatomical configuration of the esophagus, that is, lacking a serosal layer and being surrounded by loose areolar tissue, allows bacteria and digestive enzymes easy access to the mediastinum, and this leads to the development of severe mediastinitis, empyema, sepsis, and ultimately multiple-organ failure. The treatment of esophageal perforations has evolved over the past 30 years, and substantial improvements in the results are due to the use of hyperalimentation, antibiotics, and better postoperative care [2]. Nevertheless, the management of delayed or missed perforations remains controversial. We review here our experience with esophageal perforation since 1958.

Material and Methods

Classification

Esophageal perforations constitute such a heterogeneous group of injuries that some form of unifying classification is indicated. Perforations of the esophagus are classified in Table 1 according to cause, as the latter affects the clinical symptomatology, therapy, and prognosis. This is a modification of the classification of Seiler and Brooks [3]. Injuries from intraluminal agents are by far the most common and are listed first. Spontaneous perforations and perforations occurring on the basis of preexisting disease are listed separately because of the complex problems they present in diagnosis and treatment.

Patient Population

The hospital records of 64 patients treated for esophageal perforation at the University of Maryland Hospital between 1958 and mid-1989 were reviewed. There were 42 men and 22 women with a median age of 47.5 years. The cause of the perforations is shown in Table 1.

The largest number of patients, 31 patients or 48%, had perforations due to intraluminal causes (group A). The instrumentation-associated injuries resulted from endoscopy in 13 patients, dilation of strictures in 9, and attempted tracheal intubation in 2. Two perforations were caused by foreign bodies; 2, balloon dilation for achalasia; and 3, ingestion of caustic material.

The second largest group, 20 patients or 31%, had injury due to extraluminal causes (group B). Most of these patients (11) had penetrating wounds (ten gunshot wounds and one stab wound). In 3, the perforation resulted from blunt trauma (after a fall in 2 and a motorcycle accident in 1) and in 6, after a thoracic surgical procedure (hiatus hernia repair, 4; Zenker's diverticulum, 1; and ligation of esophageal varices, 1).

Group C comprised 11 patients (17%) with perforation due to Boerhaave's syndrome and group D, 2 patients (3%) with perforation caused by squamous cell carcinoma of the middle third of the esophagus.

Nineteen perforations involved the cervical esophagus, 44 the thoracic esophagus, and one the abdominal esophagus. The last was caused by a fall from a bicycle. Underlying esophageal disease was documented in 28 patients (44%). Underlying esophageal diseases that were associated with but did not cause the perforation included

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Table 1. Classification According to Cause of Perforation

Cause	No. of Patients (n = 64)	%
A. Injury from intraluminal causes	31	48
Instrumentation	24	
Endoscopy	13	
Dilation	9	
Intubation	2	
Sclerotherapy	0	
Foreign body	2	
Pneumatic injury	2	
Caustic ingestion	3	
B. Injury from extraluminal causes	20	31
Penetrating wound	11	
Blunt trauma	3	
Operative injury	6	
C. Spontaneous perforation	11	17
D. Perforations associated with preexisting esophageal disease	2	3
Tumor	2	
Esophagitis	0	

malignancy (5 patients), esophageal stricture (12), hiatus hernia (4), motility disorders (5), esophageal varices (1 patient), and compression by lymph nodes involved with Hodgkin's disease (1).

The clinical diagnosis of perforation was confirmed by contrast study with Gastrografin (diatrizoate meglumine and diatrizoate sodium) initially. When extravasation of contrast medium was not demonstrated by Gastrografin swallow, in the presence of a clinical situation highly suggestive of perforation, diluted barium was used. The perforation was missed in 5 patients (8%) in this series using Gastrografin alone. Esophagoscopy was performed mostly in patients with perforation due to traumatic injury and in patients who were suspected of having a perforation but in whom one could not be demonstrated by contrast study.

Treatment

The selection of the operative procedure is dependent on the clinical condition of the patient after the esophageal perforation. This in turn is dependent on the time interval elapsed between the onset of the perforation and therapy, and on the underlying disease. The longer the interval after the perforation, the sicker the patient and the less extensive the procedure used. Based on this presumption, patients who were diagnosed early underwent primary repair of the perforation, whereas patients with a delayed diagnosis underwent a drainage procedure, or a modification thereof, with a less favorable prognosis. Patients whose perforation was caused by an underlying disease, such as malignancy, underwent a more radical surgical procedure.

Sixty-two patients (97%) were treated surgically. Twenty-eight (45%) of the surgical patients, including all of those with perforation due to extraluminal injury (penetrating, blunt, and associated with thoracic surgical procedure), underwent primary suture closure when the diagnosis was made less than 24 hours after perforation. In 2 patients with achalasia in whom the diagnosis was made soon after balloon dilation, a Heller esophagocardiomyotomy was performed concomitantly with primary closure of the perforation.

Total esophagectomy was performed in 9 patients because of the presence of underlying disease of the esophagus: three perforations were associated with dilation of peptic strictures, three were due to necrosis of the esophagus from caustic ingestion, and three were due to malignancy of the esophagus. Two of the malignancies perforated without manipulation, whereas one perforated during gastroscopy and biopsy of an adenocarcinoma of the cardia of the stomach. Six of the esophagectomies were transthoracic and three, transhiatal. Two total gastrectomies were performed simultaneously with esophagectomy for caustic necrosis of the stomach. Colon interposition was performed in 3 patients 7 weeks to 6 months after esophageal resection.

There were five exclusion-diversion operations with a feeding jejunostomy, four in patients with perforations who were treated more than 24 hours after perforation and one in a patient whose perforation was treated within 24 hours because of the friability of the tissues. Three exclusion-diversion operations were performed for spontaneous perforations, one for delayed perforation due to a gunshot wound, and one for accidental perforation of the esophagus during mediastinoscopy for Hodgkin's disease.

Seventeen patients with late perforations underwent drainage procedures: eight cervical and nine thoracic-mediastinal. One Thal procedure was performed 2 days after a spontaneous perforation.

Two patients were treated nonoperatively because the perforations were contained, and they did not show any signs of sepsis. One was a cervical perforation that was due to a foreign body (a piece of glass) and was diagnosed late, and the other was diagnosed immediately after rigid esophagoscopy with biopsy of a peptic stricture.

Results

Because the cervical and thoracic perforations constitute the largest groups of perforations, the characteristics of each group are summarized in Table 2. The two groups appear to be homogeneous with no significant difference in age, sex, cause of perforation, time elapsed between the onset of perforation and therapy, types of operative procedures, and years of therapy. The only significant difference between the two groups is underlying disease, which is more predominant in the thoracic group (p = 0.049). The survival rate in the cervical perforation group was 16 (84%) of 19 and in the thoracic perforation group, 28 (64%) of 44 patients. No significant difference could be demonstrated between the two groups, presumably because of the small sample size (Table 3; Fig 1).

The various risk factors affecting survival are summarized in Table 3 and Figure 1. Statistical analysis was performed using the χ^2, rank sum, and Fisher's exact test (t tail) from the Statistical Analysis System. Three factors were found to affect survival: age, cause of perforation, and time interval between perforation and therapy.

Age

The median age of the survivors was 36 years compared with 56 years for the nonsurvivors ($p = 0.0127$).

Cause of Perforation

There was a significant difference in survival between group A (injury from intraluminal causes) and group C (spontaneous perforations) ($p = 0.001$) (see Fig 1). This difference is attributed partly to age differences, as the median age of group A was 46 years compared with 59 years in group C ($p = 0.033$), and partly to the underlying disease, as group A had 22 patients with underlying disease compared with none in group C ($p = 0.0001$). A significant difference in survival was also noted between group B (injury from extraluminal causes) and group C (spontaneous perforations) ($p = 0.014$). This was partly due to age differences, the median age of group B being 27.5 years compared with 59 years in group C, and partly due to the time interval between the diagnosis of the perforation and therapy. In group B, 13 of 20 patients were treated less than 24 hours after the perforation compared with 8 of 11 patients in group C treated more than 24 hours after perforation ($p = 0.044$).

Table 2. Characteristics of Cervical and Thoracic Perforation Groups

Variable	Cervical (n = 19)	Thoracic (n = 44)	p Value
Rank sum test			
Age (yr)			NS
Mean	41.5	45.6	
Median	36	50	
χ^2 Test			
Sex			
Male	14	27	NS
Female	5	17	NS
Etiology group			
A	9	22	NS
B	10	9	NS
C	0	11	NS
D	0	2	NS
Time interval			
<24 h	11	19	NS
>24 h	8	25	NS
Operation			
Primary suture	12	17	NS
Drainage	6	11	NS
Esophagectomy	0	9	NA
Exclusion-diversion	0	5	NA
Thal	0	1	NA
Nonoperative	1	1	NS
Underlying disease			0.026
Present	5	25	
Absent	14	19	
Years of therapy			0.049
1958–1974	12	16	
1975–1989	7	28	

NA = not applicable; NS = not significant.

Table 3. Factors Affecting Survival in Patients With Esophageal Perforation[a,b]

Variable	Survivors	Non-survivors	p Value
Median age (yr)	36	56	0.0127
Location			NS
Cervical	16 (84)	3	
Thoracic	28 (64)	16	
Cause			
Group A	26 (84)	5	
Group B	15 (75)	5	
Group C	3 (27)	8	
Group D	1 (50)	1	
A versus C			0.001
B versus C			0.014
Time interval			0.004
<24 h	27 (87)	4	
>24 h	18 (55)	15	
Operation			NS
Primary suture	25 (83)	5	
Drainage	10 (59)	7	
Esophagectomy	7 (78)	2	
Exclusion-diversion	1 (20)	4	
Underlying disease			NS
Present	24	6	
Absent	21	13	
Years of therapy			NS
1958–1974	19 (68)	9	
1975–1989	7	28	

[a] Numbers in parentheses are percentages. [b] Data for location and years of therapy exclude patient with abdominal perforation.

NS = not significant.

Time Interval Elapsed Between Esophageal Perforation and Therapy

There were 31 patients with esophageal perforations treated within 24 hours, with 27 survivors (87%), compared with 33 patients treated more than 24 hours after perforation, with 18 survivors (55%). Statistical analysis of the two groups demonstrated a highly significant effect of the time interval elapsed between perforation and therapy ($p = 0.004$). Survival in the group treated more than 24 hours after perforation was significantly worse.

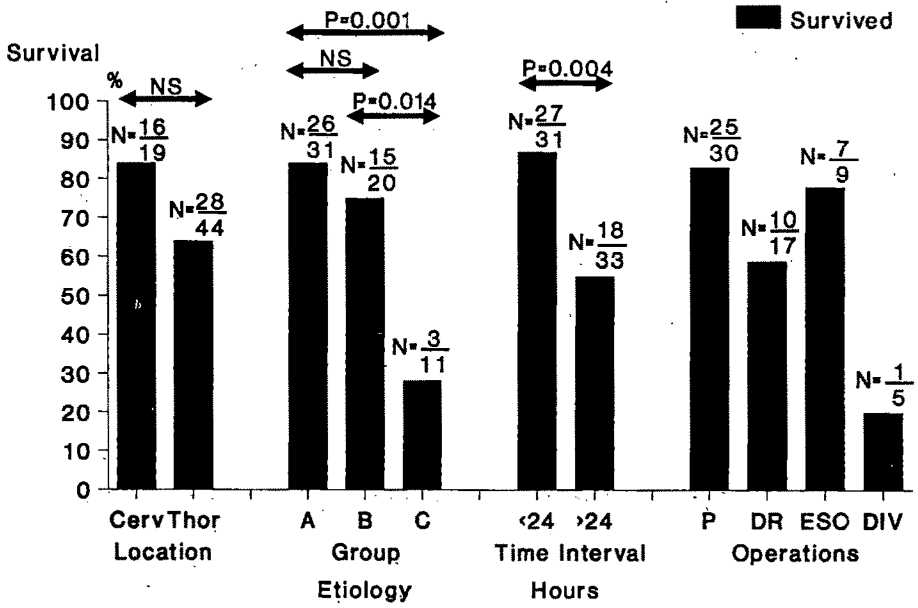

Fig 1. Significant risk factors affecting survival. (A = *intraluminal perforations;* B = *extraluminal perforations;* C = *spontaneous perforations;* Cerv = *cervical;* DIV = *diversion-exclusion;* DR = *drainage;* ESO = *esophagectomy;* NS = *not significant;* P = *primary repair;* Thor = *thoracic.)*

Comment

Over the past 30 years, certain principles have evolved in the management of acute perforations of the esophagus. Cervical perforations are mostly due to traumatic injuries resulting from gunshot wounds, stab wounds, and injuries secondary to instrumentation. The perforation frequently is diagnosed early because of the high suspicion of its occurrence, especially in the case of penetrating injuries. Confirmation of the clinical diagnosis is made by Gastrografin study, and surgical intervention is instituted without delay. Primary closure of the perforation with drainage is associated with a high success rate. Bladergroen and associates [4] reported that for 37 patients with cervical perforations, the survival rate was 90%. They attributed the improved survival after cervical perforation to be at least in part due to a greater percentage of patients being treated within 24 hours of injury. Nesbitt and Sawyers [2] documented that among 17 patients with cervical perforations, no deaths occurred in the 15 patients treated within 24 hours and two deaths in the 2 patients treated beyond this time period.

Our series confirms these reported findings. There were 10 survivors among 11 patients with cervical perforations treated within 24 hours, a survival rate of 91%, compared with 6 survivors among 8 patients treated more than 24 hours after injury, a survival rate of 75%. The overall survival for the cervical group was 16 (84%) of 19 patients. Occasionally a cervical perforation cannot be located by contrast study or esophagoscopy; nevertheless, the esophagus should be explored. When the perforation cannot be located intraoperatively, simple drainage will be adequate.

Most thoracic perforations are caused by instrumentation after endoscopy or are spontaneous. Some are due to penetrating injury, paraesophageal operation, or sclerotherapy. There is a consensus in the literature that they should be treated urgently with primary closure of the perforation and wide drainage of the mediastinum when the diagnosis is made within 24 hours of the perforation [1–3]. The wound should be covered with a well-vascularized tissue flap after closure of the perforation.

Flynn and co-workers [5] reported that 7 of 31 patients with perforations of the distal esophagus died, a mortality rate of 23%. In a study by Goldstein and Thompson [6], 44 patients had a total of 50 esophageal perforations. Twenty-three patients were treated with suture closure of the perforation and drainage. There were four deaths in this group, a mortality rate of 17%. In our series, 17 patients had primary repair of a perforated thoracic esophagus. There were three deaths, a mortality rate of 17%.

In 3 patients in our primary repair group, the primary suture repair was buttressed with a Grillo pleural flap [7], and the results were excellent in all 3. Gouge and colleagues [8] reported their experience in 14 patients with thoracic perforations in whom the suture line of closure was buttressed with a circumferential wrap of parietal pleura. All 14 patients recovered.

In recent years, muscle flaps have been used with increasing frequency. In 1985, Richardson and colleagues [9] reported that use of muscle flaps led to excellent results in 5 patients. Gouge and associates [8] summarized the results of ten reports comparing simple repair with repair with autogenous tissue buttress. In 158 simple repairs, there was a 39% incidence of fistulas and a mortality rate of 25%, and in 99 repairs with autogenous tissue buttress, a 13% incidence of fistulas and a mortality rate of 6%.

As for the management of thoracic perforations with delayed diagnosis, various modalities of therapy have been recommended. The goal of most of these procedures is to drain the infected mediastinum and pleura and to divert the esophageal and gastric secretions from these two areas. The methods include open or closed drainage of the thoracic cavity, exclusion-diversion operation [10], which entails a cervical esophagostomy, exclusion of the thoracic esophagus at the cardia, gastrostomy, and feeding jejunostomy. However, the reported results of these procedures have not been uniformly satisfactory. In a compilation of published reports on the results of these procedures [8], 58 patients treated with an exclusion-diversion procedure had a 35% mortality rate and 22 patients treated with a T tube, a 36% mortality rate. Our experience with the exclusion-diversion procedure is equally dismal. There was only 1 survivor among 5 patients, a result that led us to abandon that technique.

Other authors recommend the use of esophagectomy in the treatment of esophageal perforation. Orringer and Stirling [11] reported that 24 patients with intrathoracic esophageal perforations underwent esophagectomy with three hospital deaths (13%). In a study by Yeo and co-workers [12], 4 patients with perforations due to esophageal neoplasms were treated successfully with transhiatal esophagectomy and cervical esophagogastrostomy. We treated 9 patients with thoracic esophageal perforations by esophagectomy. The cause of the perforations was malignancy in 2, instrumentation (endoscopic biopsy of an adenocarcinoma of the cardia) in 1, caustic ingestion in 3, and dilation of peptic stricture in 3. There were two deaths, which were due to sepsis and multiple-organ failure.

We agree with Yeo and associates [12] and Orringer and Stirling [11] that transhiatal esophagectomy presents an advantageous alternative in the management of instrumental esophageal perforation adjacent to an esophageal malignancy. However, in patients without malignancy, we think that the esophagus should be preserved whenever possible. In 2 patients with achalasia in whom esophageal perforation occurred after balloon dilation, a Heller procedure was performed concomitantly with primary closure of the perforation with successful results.

Spontaneous perforation of the esophagus is a special group that presents the most serious prognosis. Delay in diagnosis accounts for the high rate of morbidity and mortality. In a retrospective review, Pate and colleagues [13] reported that 14 (41%) of 34 patients with spontaneous perforation died. There was no significant effect of delay in diagnosis on mortality, a finding contrary to that in most reported series. In their study, Rosoff and White [14] had 16 patients with Boerhaave's syndrome, 4 of whom died, a mortality rate of 25%. Eleven perforations in our series were due to Boerhaave's syndrome; only 3 of the patients had an early diagnosis (within 24 hours), and 1 survived. The diagnosis in the other 8 patients was delayed up to 10 days, and 2 survived, an overall survival rate of 3 (27%) of 11 patients.

Our experience with nonoperative management of esophageal perforations is limited to 2 patients. One had a cervical perforation due to a foreign body, and the other had a thoracic perforation after rigid bronchoscopy and biopsy of a peptic stricture in the middle part of the esophagus. Both perforations were diagnosed early and were treated with hyperalimentation and antibiotics, and both patients survived. We believe there is a limited place for nonoperative management of esophageal perforations, and that is in patients who fulfill the criteria of Cameron and co-workers [15]: the perforation must be contained, the cavity must drain back into the esophagus, and there must be no evidence of sepsis.

This study confirms the high morbidity and mortality associated with esophageal perforations despite major advances in the management of these critically ill patients. It underlines the importance of early diagnosis of the perforation and urgent treatment in the form of primary suture repair buttressed with a pleural or muscle flap. This form of therapy has been extended to the management of late perforations whenever it can be applied with reasonable success. Transhiatal esophagectomy seems to offer promise in perforations associated with malignancy or major underlying esophageal disease. Nonoperative treatment of esophageal perforations remains of limited application in a highly select group.

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DISCUSSION

DR HOOSHANG BOLOOKI (Miami, FL): I am going to discuss the group C patients, that is, patients with spontaneous rupture of the esophagus. I have been interested in such patients for some time and have experience with 24. In 1970, my associates and I published a method for repairing these lesions. The repair has worked well in our hands for a number of consecutive patients. I noted that you had 11 spontaneous perforations in the course of 30 years. The rare occurrence of this condition makes it difficult to use a uniform technique for the repair.

At the time of exploration, the perforation can look small, but in reality it involves a much longer segment of the esophagus. The extent of mucosal tear, as we suggested 20 years ago, is two to three times longer than the length of tear of the muscular layer that is visible through the thoracotomy. In fact, when the muscular layer of the esophagus is opened longitudinally, by extending the spontaneous perforation, it is possible to see that sometimes the mucosa of the gastric fundus is also involved. A primary repair of this lesion should involve separate closure of the mucosal and muscular layers after the extreme points of mucosal tear have been identified. Otherwise, primary repair of the perforation in one layer or two layers without incorporating the entire mucosal defect will most likely lead to recurrence and leakage within a week's time.

Using the technique described as the standard of repair in all patients with Boerhaave's syndrome, we have had no leakage of esophageal content and no deaths. All our patients were seen within 72 hours of the perforation, and all had varying degrees of mediastinitis at the time of operation. Currently, we do not see patients with spontaneous esophageal rupture that is a week or more old as we used to many years ago. This may be one reason for better results. Dr Attar, have you used this particular technique, and if so, what are your comments?

DR ATTAR: Dr Bolooki, I am aware of your contribution in this field (Bolooki H, Anderson I, Garcia-Rivera C, Jude JR. Spontaneous rupture of the esophagus: Boerhaave's syndrome. Ann Surg 1971;174:319–24). We have used it previously; however, in our hands as well as in the reported cases in the literature, the result of repair of spontaneous perforation is dependent on the time interval between the perforation and the repair. We believe that the earlier the surgeon can repair the perforation, with use of the pleural flap as described by Dr Grillo, the better the results will be. In a cumulative series from New York reported by Gouge and co-workers, simple repair was compared with repair with autogenous tissue buttress. Without the buttressed flap, the incidence of fistulas was 39% and the mortality rate was 25% versus a 13% incidence of fistulas and a mortality rate of 6% when the pleural flap was used. Therefore, I think your technique is acceptable, but should be supplemented with the pleural flap.

DR JOHN SAWYERS (Nashville, TN): I enjoyed Dr Attar's paper and was impressed with the good results he reported for perforations treated within the first 24 hours of recognition. At the Vanderbilt Medical Center, we have had no deaths in the last decade in 115 patients with esophageal perforations managed by operation within 24 hours of perforation. The problem, however, as Dr Attar pointed out and as seen in our data, is the patient with an intrathoracic esophageal perforation seen after 24 hours.

We have generally advocated diversion and exclusion for those patients, but I noticed that you did not have very good results with this procedure. Dr Attar, please elaborate on how you manage the intrathoracic esophageal perforation seen after 24 hours. Would you advocate esophagectomy more often for these patients?

DR KAMAL A. MANSOUR (Atlanta, GA): I enjoyed this important paper very much. It reflects a wide range of experience with a large number of esophageal perforations. This is both good and bad. It is good because of the experience gained and bad because of the number of patients with perforations, especially the iatrogenic ones, which made up more than 25% of your total. Your experience does emphasize that early diagnosis is of prime importance and is the key to increased survival and decreased morbidity.

Our experience at Emory with managing esophageal perforations is similar to yours. In the case of cervical perforations, however, we only drain and make no effort to find the tear. In distal esophageal perforations, we also use the gastric wrap routinely, not the pleural flap, and address at the same time the underlying disease process, if present. My final comment concerns traumatic perforations. There is a subgroup called "intramural perforation," something like aortic dissection. We encountered a patient with such a perforation who required no surgical intervention.

I have just one question. How did you manage the abdominal perforation, through the abdomen or through the chest?

DR JAMES W. PATE (Memphis, TN): I congratulate Dr Attar on handling a great deal of complex information on a difficult subject. It is difficult, first, because it takes 30 years to get any decent experience; this is a rare disease. Second, as has been mentioned repeatedly, the varying causes certainly represent different diseases and confuse the issues of diagnosis and treatment. It is obvious, and it has been for years, that mortality is related to the underlying disease, the mechanism of perforation, and the time delay. A patient with a delayed diagnosis and sepsis and shock certainly represents more of a risk than a patient with a clean perforation seen 1 hour after instrumental perforation of a normal esophagus.

However, I think the classic teaching that if the perforation is less than 24 hours old, we should operate and attempt to close it and if it is more than 24 hours old, we must do something extremely traumatic or just use drainage and antibiotics, is incorrect. I challenge that concept. Certainly, delay has an effect on operative mortality. However, when diagnosis of a spontaneous perforation, for example, has been delayed, closing that perforation or plugging it with a muscle flap is certainly preferable to simple drainage or exclusion of the esophagus.

I will throw out a straw man. Would you challenge the concept that all patients should have a definitive diagnosis, aggressive resuscitation, and an immediate attempt at surgical repair?

DR ATTAR: I congratulate Dr Sawyers on his excellent results. He has had 115 patients and during the past decade, has not lost a single one. I think this is due to early diagnosis and immediate repair. As for the patient with delayed perforation, primary closure buttressed with a pleural flap is recommended whenever possible. If this is not feasible, esophagectomy should then be considered.

Thank you, Dr Mansour, for your comments. Our relatively large experience is not due to our causing the perforations. Among all 64 patients, only 1 patient had a perforation that was caused by one of us during dilation of a stricture; the perforation was recognized immediately, and the patient was treated nonoperatively and lived. The patient with the abdominal perforation had received other injuries in the abdomen at the same time. The perforation was, of course, repaired intraabdominally.

Dr Pate, I know you have challenged the concept of delay in repair of esophageal perforation, especially in the spontaneous group. Nevertheless, we believe that early diagnosis and immediate repair is the recommended treatment. The reason for this is very simple. The longer the time elapsed between the perforation and the repair, the more mediastinal inflammation and spread of infection occur. Therefore, it stands to reason that the earlier the repair is done, the better the results obtained will be.

Notice From the Southern Thoracic Surgical Association

The Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Cerromar Beach, Puerto Rico, November 8–10, 1990. There will be a $155 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 8, 1990. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Advance registration forms, hotel reservation cards, and details regarding transportation arrangements will be mailed to Association members. Nonmembers should write to the Secretary-Treasurer, Gordon F. Murray, MD.

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Management of the Ectopic ACTH Syndrome Due to Thoracic Carcinoids

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Mark Stovroff, MD, John Vetto, MD, Jeffrey A. Norton, MD, William Travis, MD,
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The association of a bronchial or thymic carcinoid as a source for the ectopic production of adrenocorticotropic hormone (ACTH) has been reported since 1957, with approximately 72 cases in the literature. These patients are characterized by young age, long duration of Cushing's syndrome because of the inability to find the ectopic source, and a high incidence of hypophysectomy or adrenalectomy without curing the disease. A substantial number of patients, upon discovery of the thoracic ectopic source, are also found to have malignant carcinoid tumors with lymph node metastases. Fifteen patients have been explored for a presumed intrathoracic source of ACTH at our institution since 1983 and 14 carcinoids (13 bronchial, one thymic) have been resected. Seventy-one percent (10/14) of the patients appear cured with normal plasma ACTH levels 5 to 57 months after resection, despite a 50% incidence of positive lymph node disease. Management of these patients demands an aggressive evaluation to prevent unnecessary adrenalectomy or hypophysectomy and to allow earlier resections before these potentially curable malignancies metastasize. When the tumor is discovered, thorough exploration and complete lymph node mapping with resection must be performed.

(Ann Thorac Surg 1990;50:52–7)

It is rare that thoracic surgeons are consulted to evaluate patients with hypercortisolism; however, between 10% and 15% of patients with Cushing's syndrome will have ectopic production of adrenocorticotropic hormone (ACTH) by a nonpituitary tumor [1]. Usually, in cases of malignant bronchial neoplasms, such as oat cell carcinoma, the cause is obvious. There are, however, a group of patients who are seen with the ectopic production of ACTH in whom the ectopic source of ACTH cannot be localized despite roentgenographic attention to the adrenal glands, pancreas, pituitary gland, and chest [2, 3]. These patients are at risk of death due to sepsis, gastrointestinal perforation, and metastatic dissemination, and it is generally felt that they have the most severe form of endogenous hypercortisolism. Adrenalectomy may be required if the source is not found, and even after adrenalectomy the development of metastases from the unknown source may occur.

For editorial comment, see page 5.

The association of ectopic ACTH production with intrathoracic carcinoid tumors is not a new one [4]. The rarity of the syndrome, however, despite the gravity of the problem, has made the study of this entity by a single institution difficult. We have studied the ectopic ACTH syndrome since 1975 in an effort to elucidate the biochemical, roentgenographic, and pathological aspects of the syndrome. This report describes 15 patients who have had a thoracotomy for a presumed intrathoracic source of ectopic ACTH since 1983, and represents the largest operative series of intrathoracic carcinoid tumors causing Cushing's syndrome from a single institution. This series illustrates the difficulty in preoperative localization of the ACTH source, comments on newer localization techniques, and describes the surgical management of these patients. A review of the world's literature since 1957 with specific attention to the association of Cushing's syndrome and bronchial carcinoids is also summarized.

Material and Methods

Since 1981, 33 patients have been evaluated by the Endocrine Branch of the National Institutes of Health (NIH) with a presumptive diagnosis of ectopic ACTH syndrome. Of these, 15 patients have had thoracic exploration for the ectopic source. The diagnosis of Cushing's syndrome was established by the presence of hypercortisolism and high 24-hour urinary free cortisol levels. Pituitary dependence or independence was assessed by the 6-day, low-dose and high-dose dexamethasone suppression test and the metyrapone stimulation test as described by Liddle and associates [1], as well as the ovine corticotropin-releasing hormone (CRH) stimulation test [2, 3]. Plasma ACTH

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levels as well as tumor tissue ACTH levels in specific cases were obtained. Chest roentgenography was performed in all patients. Computed tomography of the abdomen, pituitary glands, and chest was performed initially and in some cases serially until a thoracic source appeared. Inferior petrosal sinus sampling was performed since 1982 in patients in whom the radiographic studies failed to reveal a unilateral adrenal mass [5]. Briefly, petrosal sinus sampling involves the bilateral simultaneous sampling of both petrosal sinuses and a peripheral vein for plasma ACTH levels before and after the administration of ovine CRH. This permits comparison of the ACTH levels from both sides of the pituitary and the periphery. Patients with an ectopic source of ACTH do not have a gradient in ACTH levels between the periphery and petrosal samples. In contrast, patients with an ACTH-secreting pituitary tumor have petrosal levels of ACTH greater than peripheral levels, and this petrosal to peripheral gradient increases after CRH administration.

Computed chest tomography was performed, obtaining 5-mm contiguous sections from the pulmonary apices to below the costophrenic sinuses, with contrast enhancement if there were no contraindications to its use. Magnetic resonance imaging was performed in 7 patients with 10-mm contiguous transaxial sections from the pulmonary apices to the costophrenic sinuses with occasional coronal sections.

All patients had endocrine evaluation at the NIH, and 14 of the 15 patients had thoracic exploration at the NIH. All thoracotomies were performed under steroid coverage with use of preoperative antibiotics and single-lung ventilation. In all cases, complete exploration of the pulmonary parenchyma was performed via median sternotomy or lateral thoracotomy, with nodal basin evaluation with frozen section analysis of suspicious nodules.

A review of the world literature from 1957 to 1989 with regard to the association of Cushing's syndrome with bronchial/thymic carcinoids was performed [1, 2, 4, 6–37]. These reports were analyzed for clinical, biochemical, and roentgenographic characteristics available at the time of the publication. Operative procedures, as well as the performance of concomitant lymph node dissection, and long-term survival were recorded as best could be deduced.

Results

Symptoms and Biochemical Data

The 8 female and 7 male patients had a mean age of 37 ± 4 years with a range of 11 to 70 years. The mean duration of Cushing's syndrome from the time of diagnosis to thoracic exploration was 52 ± 17 months (range, 8 to 264 months). Before the NIH admission, 6 patients (40%) had had a previous surgical procedure (hypophysectomy, 3; adrenalectomy, 2; adrenalectomy and hypophysectomy, 1).

A triad of weakness, Cushingoid features, and hypokalemic alkalosis was present in 14 of the 15 patients (93%). All patients had elevation of their serum cortisol to greater than 770 nmol/L (28 μg/dL), and 14 of the 15 patients had elevation of their urinary free cortisol excretion to greater than 110 μg/24 hours. A peripheral venous sample for ACTH was elevated to 44 pmol/L (200 pg/mL) or more in 12 of the 15 patients (80%). Petrosal sinus sampling and CRH testing was performed at the NIH in 14 patients. These patients had no central step-up of petrosal sinus ACTH levels and no stimulation of ACTH levels after CRH administration.

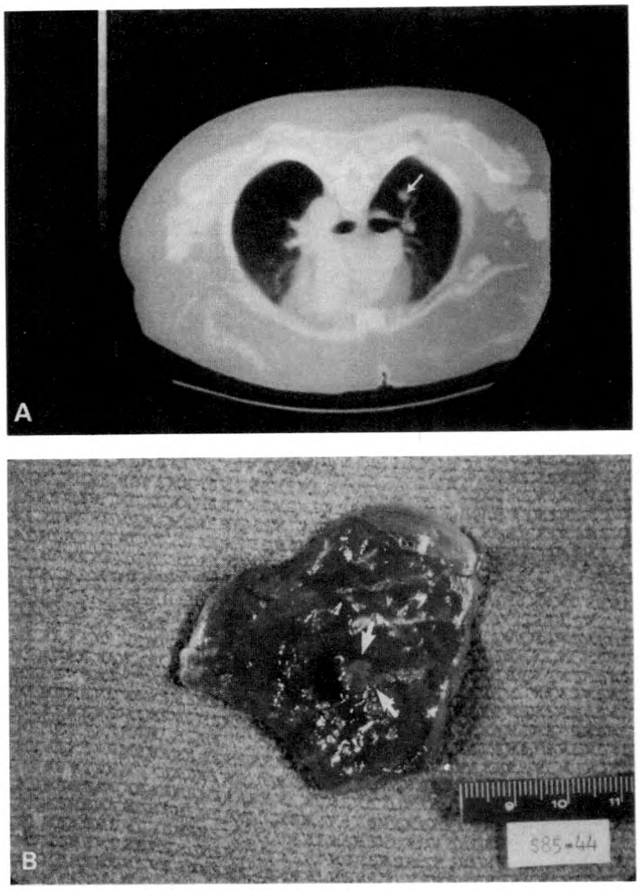

Fig 1. (A) Appearance of preoperative computed tomographic scan depicting right upper lobe nodule (arrow). *(B) Preliminary wedge excision of right upper lobe nodule revealed bronchial carcinoid* (arrow). *Lobectomy and lymph node dissection were then performed.*

Roentgenographic Data

Computed tomography of the pituitary did not show evidence for a pituitary ACTH source in any patient. Preoperative abdominal CT revealed bilateral adrenal hyperplasia in 11 of the 12 patients with intact adrenal glands scanned. No evidence for pancreatic or adrenal neoplasms was seen in any patients.

Chest roentgenograms were normal before resection in 10 of the 15 patients; 4 of 5 patients with an abnormal roentgenogram were found to have a nodular density, and one had evidence of focal thymic enlargement. Computed tomography of the chest revealed a single nodular density in 12 patients and a thymic mass in 1, and was unrevealing in 2 patients (Fig 1). There were 12 true-positive CT scans, one true-negative, one false-negative, and one false-positive for an accuracy of 87% and a positive predictive index of 92%.

Magnetic resonance imaging scanning of the chest performed in our last 6 patients confirmed a nodule seen by CT, and the nodule was enhanced intensely on the short inversion recovery (STIR) sequence in 5 patients. One nodule that was not revealed by CT was seen on magnetic resonance imaging. Five of the six nodules were the ectopic source, with one false-positive (loculated pleural fluid).

Surgical Approach and Extent of Resection

Seventeen operations were performed in 15 patients. All patients had bronchoscopy before resection that failed to reveal an endobronchial abnormality. The first 8 patients were explored by lateral thoracotomy whereas the last 7 patients had median sternotomy. A bronchial carcinoid tumor was seen on frozen section in 13 of the 15 patients. Twelve patients had a lobectomy: right upper, 4; middle, 3; right lower, 2; left lower, 2; and left upper, 1. Of these, five were performed by median sternotomy.

The first patient in this series had wedge resection without lymph node dissection, and all subsequent patients with evidence of bronchial carcinoid tumor have had regional lymph node dissection including the mediastinal nodes in addition to the lobectomy. The 1 patient with thymic carcinoid tumor underwent total thymectomy and lymph node dissection.

Morbidity and Mortality

All patients were extubated on the operative day. There were no infectious complications. Two patients required elevation of their steroid replacement postoperatively for cortisol insufficiency based on symptoms and plasma cortisol levels.

There was one postoperative death in a 57-year-old patient biochemically cured of his disease who had cortisol levels less than 28 nmol/L (1 μg/dL) on routine steroid replacement. This patient had a sudden cardiac arrest during the placement of a central line and autopsy revealed severe coronary atherosclerosis and evidence of myocardial infarction.

Immediate Effects of Cortisol Levels

Ten of the 14 patients who underwent resection had immediate (24 to 36 hour) evidence of decreasing ACTH levels. Cushingoid features routinely resolved within a 6- to 8-month period.

Four patients did not have decreased ACTH levels after operation. One patient in whom an ACTH-positive bronchial carcinoid tumor was found was not cured despite lobectomy and lymph node dissection. She has been reexplored twice with negative lymph node dissections and lung palpation but no additional ectopic source has been found. Two other patients did not become eucortisolemic after operation despite the finding of a bronchial carcinoid. One patient (the first in the series) had simple wedge excision without lymph node dissection and subsequently experienced depression during postoperative steroid withdrawal and committed suicide. A 15-year-old boy who had an adrenalectomy before the carcinoid was resected had positive mediastinal nodes and is at present persistently hypercortisolemic. An 11-year-old girl with elevated thymic vein ACTH levels and "tumor blush" on angiography was found to have a thymic parathyroid and was not cured of her hypercortisolism.

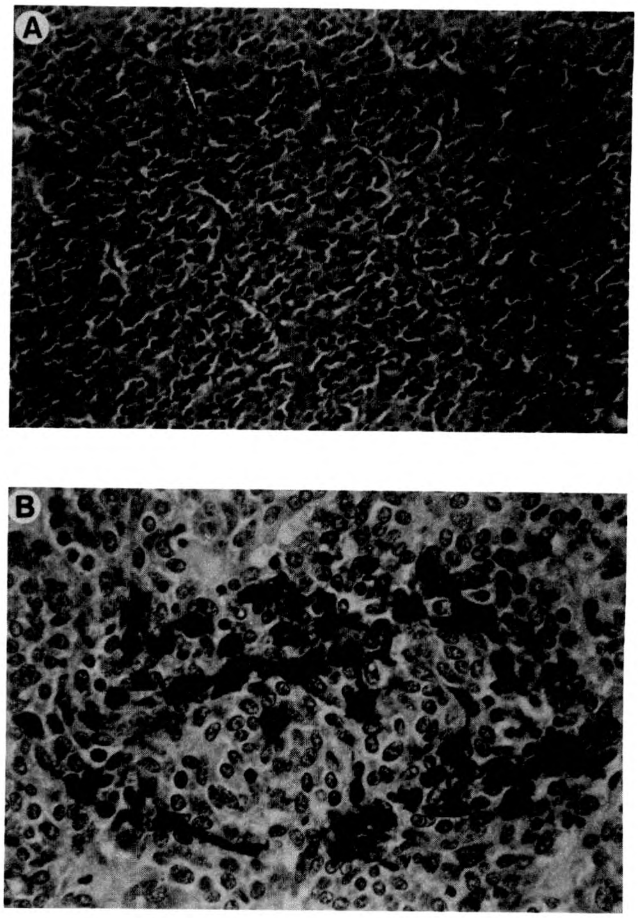

Fig 2. (A) This bronchial carcinoid tumor is characterized by nests of cells with a moderate amount of eosinophilic cytoplasm in nuclei showing finely granular chromaffin. (Hematoxylin and eosin, ×250 before 22% reduction.) (B) Positive immunohistochemical stain of same tumor as in (A) for adrenocorticotropic hormone.

Pathological Findings

Characteristic histological features of carcinoid tumors were present in each patient (Fig 2A). The mean size of the 13 resected bronchial tumors was 1.1 ± 0.2 cm (0.3 to 2.5 cm). The tumors were composed of sheets and nests of uniform cells with moderate eosinophilic cytoplasm and finely granular nuclear chromatin. Twelve of the bronchial tumors were typical carcinoids and one was an atypical carcinoid according to criteria proposed by Arrigoni and co-workers [38]. The thymic tumor resembled an atypical carcinoid tumor. Immunohistochemistry for ACTH was positive in all cases (Fig 2B). Electron microscopy was performed in 13 cases and revealed dense-core neuroendocrine granules in the cytoplasm of the tumor cells.

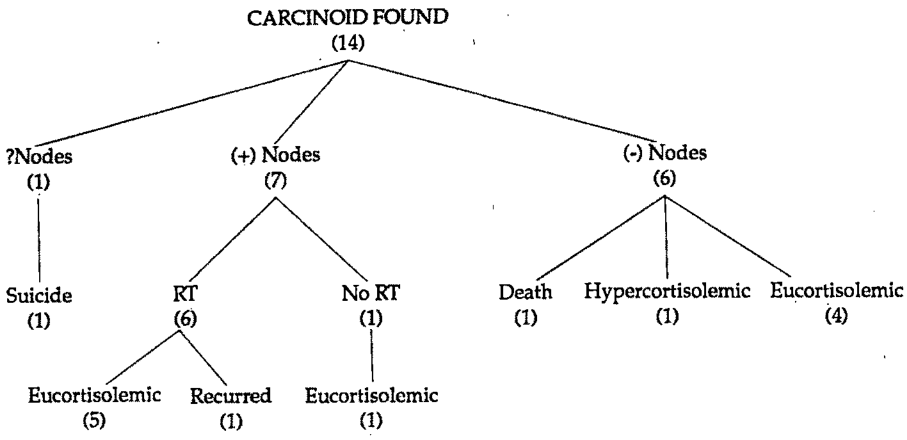

Fig 3. Results of surgical management in the 14 patients with hypercortisolism from a thoracic source. (See text for details.) (RT = *radiation therapy.)*

Follow-Up

Of the 14 patients originally found to have a carcinoid, 12 are alive at a mean of 21 ± 4 months after resection (range, 5 to 57 months) (Fig 3). Ten (71%) are presently eucortisolemic. Ten of the patients in whom a carcinoid was found became eucortisolemic immediately after operation; 5 of these 10 were found to have positive mediastinal adenopathy. Seven patients in the series had metastases in mediastinal lymph nodes. Six of these received postoperative mediastinal irradiation. Levels of ACTH are now normal 8 to 31 months after resection in 5 of the 6. One patient, whose plasma ACTH level did not normalize immediately after operation, is presently eucortisolemic with normal ACTH levels 8 months after radiation therapy. The patient with thymic carcinoid and mediastinal metastases originally became eucortisolemic; however, despite postoperative radiation therapy his cortisol levels rose and he was found to have a recurrence outside the radiation portal 13 months later. He is presently alive with evidence of disease.

Literature Review

Tables 1–3 reveal the clinical, biochemical, and surgical profiles of 72 cases documented in the literature to have Cushing's syndrome in association with a bronchial or thymic carcinoid. Complete clinical and surgical data were available for all 72 patients. Briefly, as reported in the present series, these patients were characterized by young age, hypokalemic alkalosis, Cushing's syndrome, and elevated ACTH levels. Many had previous ablative pituitary or adrenal operations in an attempt to cure their Cushing's syndrome, usually because of mistaken diagnosis. A high rate of lymph node disease (24%) was detected at the time of thoracic exploration. Immediate biochemical and later clinical resolution of the hypercortisolism was possible in the majority of patients whose disease was completely resected and for whom these follow-up data were available.

Table 1. Bronchial Carcinoids and Cushing's Syndrome, 1957–1989: Clinical Characteristics (n = 72)

Characteristic	Value
Age (yr)	41 ± 2 (15–74)[a]
Sex (F/M)	41/31
Symptoms/signs	
Cushingoid habitus	97%
Weakness	93%
Weight gain	88%
Edema	93%
Hypertension	93%
Hyperpigmentation	49%
Duration of symptoms (mo)	36 ± 6 (1–240)[a]

[a] Values in parentheses are range.

Comment

An association of Cushing's syndrome with bronchial carcinoid has been known since 1957, and a lobectomy with resolution of Cushingoid habitus was performed in 1960 [6]. The work-up of the patients with ectopic ACTH has been radically altered by the use of invasive and noninvasive radiographic techniques, specifically inferior petrosal sinus sampling, which can document the absence of a gradient between the inferior petrosal sinus samples and peripheral ACTH samples and confirm an ectopic source.

The evolution of techniques in the radiographic evaluation of these patients illustrates the desire to more efficiently localize the ectopic source. At our institution, patients with the ectopic ACTH syndrome undergo CT scanning of the chest and abdomen, searching for an

Table 2. Bronchial Carcinoids and Cushing's Syndrome, 1957–1989: Biochemical Data (n = 45–65)

Variable	Percent
Hypokalemic alkalosis	72
Serum cortisol elevation	93
Urinary free cortisol elevation	98
Plasma ACTH elevation	54
Positive dexamethasone suppression	41
Metyrapone stimulation	60

ACTH = adrenocorticotropic hormone.

Table 3. Bronchial Carcinoids and Cushing's Syndrome, 1957–1989: Operative Data (n = 72)

Variable	Percent
Previous operation	
Adrenalectomy	38
Hypophysectomy	17
Diagnosis/resection	
Thoracotomy	68
Autopsy	18
Roentgenography only	10
Bronchoscopy	1
Lymph node biopsy	3
Nodes positive	24

adrenal or foregut source. In the absence of abnormal scans or biochemical markers for tumors, patients are placed on drugs that suppress steroidogenesis (ketoconazole, aminoglutethimide, or metyrapone) or a glucocorticoid antagonist (RU486) as a temporizing measure. Frequently, small radiographic abnormalities appear with time or, in retrospect, were present at the inception of the evaluation.

We have found the contrast-enhanced chest CT with 5-mm contiguous sections to be the most useful procedure in localizing these tumors, with a high positive predictive index. More recently, however, magnetic resonance imaging with the STIR sequence has not only confirmed the CT findings but detected a pulmonary nodule undetected by CT. On the T2 or STIR sequence, the tumor appears bright and the blood vessels dark.

The surgical management of patients with a thoracic ectopic source for ACTH is guided at the NIH by three principles: (1) complete exploration at a single operation, (2) anatomical resection of the involved lobe/thymus, and (3) compulsive lymph node resection. The inability to cure 2 patients despite localization of a bronchial carcinoid implies inadequate resection of all malignant ACTH-secreting carcinoid tumor. In 1 patient who had a simple wedge excision without lymph node dissection, high ACTH levels persisted requiring adrenalectomy, after which the patient committed suicide. Moreover, 24% of the patients in the literature have been noted to have lymph node disease at the time of resection, and this finding appears to be an underestimation of the 54% of our patients having positive lymph node disease in whom a carcinoid was found. We recommend, therefore, complete lymph node dissection in all cases, not only for eradiction of the syndrome but possibly to prevent dissemination of this malignancy. Indeed, a complete resection of tumor is accompanied by a precipitous fall of ACTH levels into the normal range.

The approach of median sternotomy or thoracotomy will, of course, depend on the individual surgeon's preference. We routinely use the median sternotomy approach, however, to accomplish pulmonary venous sampling from all lobes and to perform complete bilateral exploration. The lobectomies and lymph node dissection are performed through this approach with subaortic and preaortic lymph node removal on the left, subcarinal dissection for lesions on either side, and right paratracheal, superior mediastinal, and azygous dissection on the right. If the radiographic abnormality does not prove to be the carcinoid tumor (as occurred in 1 patient), meticulous exploration of all lobes and lymph node basins should be performed with liberal use of frozen section to find the ectopic source elsewhere in the chest.

The malignant potential of these carcinoids is well established in the literature and is reinforced by our series. Long-term survival after lymph node dissection and primary resection is possible with complete excision. We have used postoperative radiation therapy empirically in the group of patients with positive lymph node disease, chiefly for local control. It is too early in this particular series to document long-term efficacy; however, the presence of a natural marker (ACTH) will allow us to assess recurrence easier and earlier than in the usual patient with non-small cell lung cancer. Patients are monitored for biochemical and roentgenographic abnormalities every 6 months after resection either by the NIH or by the referring endocrinologist.

In conclusion, primary surveillance of the chest should be performed in all patients with clinical and biochemical suspicion of an ectopic ACTH source, as the majority of the patients with this syndrome will have intrathoracic pathology. Evaluation with petrosal sinus sampling and CRH stimulation will point to an ectopic source, and CT and magnetic resonance imaging may reveal a hitherto unsuspected abnormality. Exploration with lobectomy and lymph node dissection is justified in this group of patients to avoid subsequent adrenalectomy and to document the stage of disease. The role of radiation therapy postoperatively is not clearly defined, but in patients with lymph node disease, persistent local control with normal ACTH levels may be achievable. An aggressive approach to diagnosis and therapy of these patients may speed the localization of the ectopic source and lead to a gratifying resolution of clinical and biochemical stigmata of hypercortisolism.

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DISCUSSION

DR SAFUH ATTAR (Baltimore, MD): I would like to congratulate Dr Pass on a very fascinating series and to ask him a couple of questions. There has been a recent consensus in the pathology literature that the carcinoid is a single entity, whether it occurs in the lung, in the thyroid, or in the thymus. There have been reported cases of carcinoid in the ovary, uterus, and fallopian tubes that have been detected with increased ACTH secretions. My question is, do you believe that in the new theory there is an anlage to the carcinoid disease that occurs in the various organs throughout the body, including the lung, the thyroid, the thymus, and the pelvis? Have you checked in any of your patients whether the ovary or the uterus were involved with such a tumor? Second, was there any correlation between the benign or malignant character of the tumor and the production of ACTH?

DR PASS: We perform CT scanning of the abdomen routinely to look for other sources in working up these patients. We have not found any patients in the series so far, including the ones that are still being followed up, with any pelvic abnormality, although that has been reported. Most of these carcinoids will occur in the lungs or the thymus. We have not correlated, as Dr Benfield does with his elegant studies of fluorescence-activated cell sorting analysis of the carcinoids, changes in the carcinoids that predict which tumor may be worse than another. But we do subscribe to the theory that there is a spectrum of carcinoids that are neuroendocrine tumors. I personally think that the carcinoids with ACTH activity or any endocrine activity should be regarded as different, that is, malignant, and therefore have a high incidence of lymph node metastases. They require complete resection and are different from the classic bronchial carcinoid.

Carcinoid Tumors of the Thymus

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Carcinoid tumors arising in the thymus are rare. Since Rosai and Higa in 1972 distinguished these neoplasms from thymomas, fewer than 100 cases have been reported in the world literature. In a 38-year review (1950 to 1988) of surgically treated thymic tumors at Henry Ford Hospital, only 7 cases of thymic carcinoids were identified. These 6 men and 1 woman ranged in age from 27 to 70 years (mean, 48 years) at diagnosis. Follow-up was available in all patients with the longest survival being 12 years in 2 patients, and the shortest, 1 year, in 1. Recurrences and/or metastases developed in 4 of 7 patients between 1 and 9 years after initial resection. Recurrences were treated by reexcision in addition to radiation treatment and chemotherapy in 3 patients and reexcision with radiation treatment alone in 1 patient. A review of the literature along with our experience suggests that thymic carcinoids have a biological behavior distinct from thymoma in terms of cell origin, associated syndromes, neoplastic behavior, and prognosis. An aggressive surgical approach with complete initial excision of the tumor and of subsequent recurrences, along with radiation and probably chemotherapy, is the best available treatment today.

(Ann Thorac Surg 1990;50:58–61)

In 1972 Rosai and Higa [1] described thymic carcinoids as a separate entity from thymomas. Since then, these tumors have been the subject of case reports [2–20]. Only a few authors have reported a substantial number of cases, precluding assessment of biological behavior, the efficacy of various treatment modalities, and long-term survival of these patients [21, 22]. The results of initial treatment and therapy of recurrence and long-term prognosis in 7 patients with thymic carcinoids from our institution along with review of the literature are herein reported.

Material and Methods

During a 38-year (1950 to 1988) review of thymic tumors at Henry Ford Hospital, we found 7 cases of thymic carcinoids. The diagnosis in 3 of the patients (1965 to 1976) was made on review of the histological material from excised recurrent tumors 1, 4, and 9 years after the initial operation. In the remaining 4 patients, the diagnosis was made by histological study (light microscopy, immunohistochemistry, and/or electron microscopy) of the specimens removed at the initial operation.

For editorial comment, see page 5.

Results

Clinical Findings

In the 7 patients (6 men, 1 woman) age ranged from 27 to 70 years at the time of diagnosis (Table 1). The presenting complaints were abdominal pain and diarrhea in 2 patients, shortness of breath and chest pain in 2, and pericarditis in 1; 1 patient was totally asymptomatic. None of the patients had manifestations of either other endocrinopathy or the carcinoid syndrome. Hydroxyindolacetic acid studies on the 2 patients with diarrhea were negative. One patient had a history of previous excision of medullary thyroid carcinoma 15 years before the thymic tumor was found. Physical findings were normal in all patients at their initial presentation. All patients had evidence of an anterior mediastinal mass by chest roentgenogram, tomograms, and computed tomographic scans of the chest (in 3 patients). Aortograms performed in 3 patients were unremarkable.

Findings at Operation

A well-confined, encapsulated mass in the thymic region was found in 2 patients; in the remaining patients the tumor was invading adjacent mediastinal structures (innominate vein, pleura, pericardium, lung, and phrenic nerves). The size of the tumor ranged from 3 to 10 cm in diameter. Preliminary biopsy was performed in 1 patient via mediastinotomy.

Treatment and Follow-up

Six patients had their tumor removed through a median sternotomy and one tumor was approached through a right thoracotomy.

Grossly the tumor was totally removed in all patients along with adjacent structures when invasion was seen (wedge lung resection, pericardium, phrenic nerve, innominate vein, lymph nodes) (Table 1; Fig 1).

After the pathological diagnosis was made (Fig 2), 6 patients received adjuvant radiation treatment and 1 received chemotherapy with 5-fluorouracil and streptozotocin. Recurrence developed in 4 patients at 1 to 9 years after the initial excision (Table 2). There were four docu-

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Table 1. Findings at Operation and Initial Treatment of Thymic Carcinoid Patients

Patient No.	Age (yr)	Sex	Findings at Operation	Initial Treatment
1	36	M	Thymic tumor (10 × 5 cm) invading innominate vein, left pleura, and pericardium	Excision of thymus, innominate vein, left mediastinal pleura, and pericardium; adjuvant irradiation (46 Gy)
2	40	M	Encapsulated thymic tumor	Thymectomy
3	40	M	Thymic tumor attached to left pleura	Excision of tumor and adjacent pleura
4	70	M	Encapsulated thymic tumor	Thymectomy
5	27	M	Encapsulated tumor	Thymectomy; radiation treatment, 5FU, streptozotocin
6	69	F	Invasion of innominate vein	Excision of tumor and innominate vein
7	53	M	Invasion of left pleura and medial surface of LUL	Excision of tumor, lung wedge resection

5 FU = 5-fluorouracil; LUL = left upper lobe.

mented recurrences in 1 patient, all of them excised, and 2 of the patients had two operations for recurrences. All patients received irradiation (46 Gy) and chemotherapy with 5-fluorouracil, streptozotocin, and carmustin (BCNU) after removal of the recurrent tumor. One patient had brachytherapy with iodine 125 after debulking of the recurrent tumor. Recurrent tumors were detected in the mediastinal structures, lung, and adrenal glands.

Two surviving patients are being followed yearly with chest roentgenograms and computed tomographic scans. Autopsies were performed in 4 of the 5 patients who died. Findings on autopsy consisted of carcinoid tumor disseminated to the mediastinum, lung, pleura, and abdomen with only 1 patient having no evidence of recurrence. Survival after the initial diagnosis and treatment of thymic carcinoids ranged in our series from 1 to 12 years with a median survival of 2 years.

Comment

Carcinoid tumors of the thymus were first recognized in 1972. Since then, and from reports by other authors, the pathological and clinical characteristics of this tumor revealed a totally different entity from the thymoma (Table 3). The pathological diagnosis of thymic carcinoids is based on findings from light microscopy, histochemical studies, and electron microscopy [1, 14, 21, 22].

Review of the literature revealed that almost 50% of thymic carcinoids are seen with endocrinopathies, namely, Cushing's syndrome, multiple neoplasia I and II, or

Table 2. Recurrence(s) and Treatment Received in Thymic Carcinoid Patients

Patient No.	Age (yr)	Sex	Date of Initial Operation	Date of Recurrence	Site of Recurrence	Treatment Received
1	36	M	8/65	6/69	Sternum, pleura, SVC syndrome	Irradiation
2	40	M	9/69	5/74	RLL, hilum	RLL lobectomy, irradiation
				2/77	Chest wall, neck LN	Excision, irradiation
				11/177	Chest wall	Excision
				11/80	Left adrenal glands	Adrenalectomy, liver biopsy (−), irradiation, 5FU, streptozotocin
4	70	M	8/76	2/77	Paraesophageal LN, neck	Excision, irradiation
				9/77	Pleura, neck	Irradiation
5	27	M	4/77	4/82	Chest wall	Excision, irradiation
				1/85	Mediastinum	Debulking, brachytherapy (I^{125})

5FU = 5-fluorouracil; LN = lymph nodes; RLL = right lower lobe; SVC = superior vena cava.

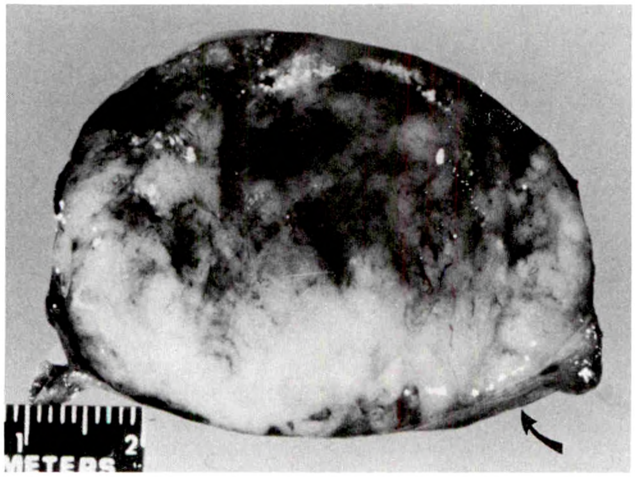

Fig 1. Gross appearance of the tumor showing highly vascularized bulging cut surface. Arrow *indicates attached pericardial surface.*

inappropriate antidiuretic hormone secretion, in that order of frequency [5, 14, 16, 21, 22, 23]. Other associated syndromes reported with this tumor are polymyositis [4], clubbing [4], polyarthropathy [4], and pericarditis [15]. The male predominance of this tumor is striking (more than 90% males), and in none of the reported cases so far has the carcinoid syndrome been present.

When not associated with an endocrine syndrome, the most common presentation of a thymic carcinoid is that of an anterior mediastinal mass, although a posterior mediastinal thymic carcinoid has been reported [20]. A chest roentgenogram and computed tomographic scan reveal details about the tumor, possible invasion of the surrounding structures, and intrathoracic metastases. One of the characteristics of the thymic carcinoid is the frequency of extrathoracic metastases (20% to 30%) [5, 14, 21–23], which can be widely spread involving skin, bone (osteoblastic), lymph nodes, and adrenal glands (our own patient), in contrast with thymomas, in which extrathoracic metastases are very rare (see Table 3).

An association between extracapsular invasion of mediastinal structures at the initial exploration and Cushing's syndrome on clinical presentation with worse prognosis has been implied [5, 14, 23]. Our literature review revealed only two series of patients with thymic carcinoid who were treated and followed up for a long time [21, 22]. The survival after the initial diagnosis and treatment varied from 1 to 15 years, and the majority of the patients had repeated operations for metastases and local recurrences.

In our series, the approach to this tumor was the same as any other anterior mediastinal tumor, ie, exploration and excision. Every effort was made to remove the entire tumor along with surrounding structures if invasion was found. Because the diagnosis of thymic carcinoid requires pathological confirmation, most patients are initially thought to have had a thymoma removed. After the diagnosis of thymic carcinoid, adjuvant radiotherapy consisting of a total of 46 Gy was given in all patients that had invasion of the surrounding structures. In one of our patients chemotherapy (5-fluorouracil, streptozotocin) was also instituted. A similar treatment protocol was used in two other series of thymic carcinoids. Follow-up consisted of clinical examination, chest roentgenogram, computed tomograms, and metastatic workup every 6 to 12 months [21, 22].

Recurrence and extrathoracic metastasis are characteristic of thymic carcinoids, and as in the other series, our longest survivors had reoperations for removal of intrathoracic recurrences or extrathoracic metastases (one of the patients required four excisions!) followed by addi-

Fig 2. Trabecular arrangement of tumor cells (left; hematoxylin and eosin ×235), positive cytoplasmic stains for chromograin (upper right; avidin-biotin complex immunoperoxidase, ×235), and neurosecretory granules (lower right; electron microscopy). (All magnifications before 28% reduction.)

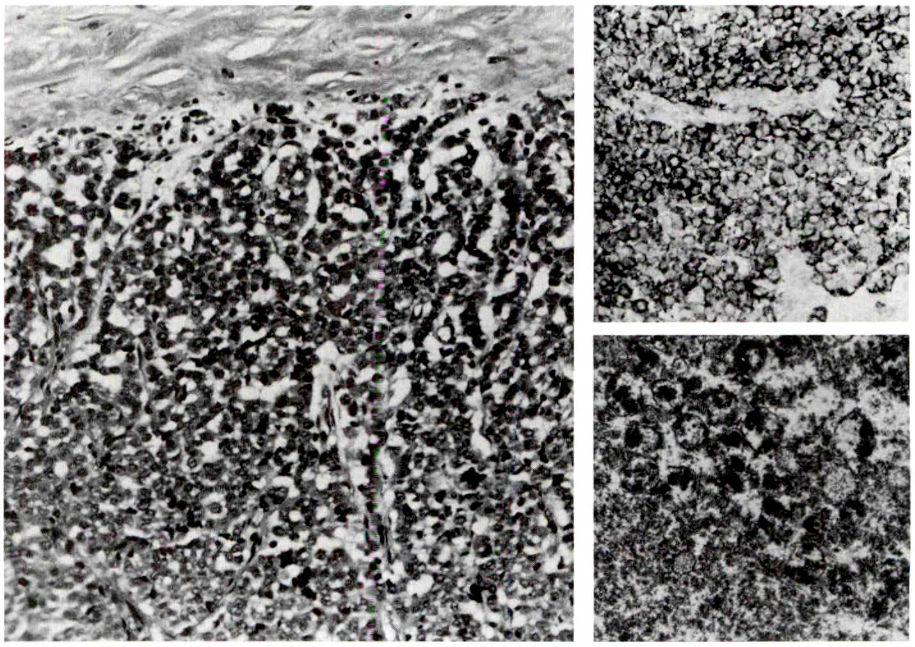

Table 3. Differences Between Thymic Carcinoid and Thymoma

Feature	Thymic Carcinoid	Thymoma
Progenitor cell	Neuroendocrine cells of neural crest origin	Epithelial cells of bronchial pouch derivation
Associated syndromes	Cushing's syndrome, MEA-1, MEN-2, pericarditis, polyarthropathy, clubbing, myositis	Myasthenia gravis, red cell aplasia
Metastases	30% extrathoracic skin, bones (osteoblastic), adrenal glands	Rare extrathoracic
Invasion of surrounding thoracic structures	50%	10%
Prognosis	Poor, with recurrences and metastases years after excision. Not easily controlled by irradiation or chemotherapy	Cure in stage I (encapsulated) thymoma. Controlled by irradiation and/or chemotherapy in stages II and III

MEA-1 = multiple endocrine adenomatosis-1; MEN-2 = multiple endocrine neoplasia-2.

tional irradiation and chemotherapy for widespread metastases.

Long-term follow-up of the patients in our series and others revealed that thymic carcinoids have a rather poor prognosis based on their tendency to recur and metastasize widely many years after the initial excision [21, 22]. Long-term survival can only be achieved by aggressive excision not only of the initial tumor but of subsequent recurrences and metastases. The role of adjuvant radiotherapy and chemotherapy is still uncertain [24], but radiotherapy should be considered because the behavior of this tumor is uncertain and recurrences can occur even years after the initial excision.

In conclusion, thymic carcinoid is a rare tumor, totally different from the ordinary thymoma, with a poor prognosis. It is frequently associated with endocrinopathies and has a characteristic tendency for recurrence and metastases many years after the initial diagnosis and treatment. Surgical extirpation of the tumor initially and of the subsequent recurrences is the most effective treatment today. Radiotherapy seems to be helpful in most of the cases. The role of chemotherapy at this time is uncertain.

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Acute Preoperative Plasmapheresis and Established Blood Conservation Techniques

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Plasmapheresis performed weeks before an operation producing autologous plasma has proved to be of benefit in elective operations. First experiences in acute plasmapheresis, which is performed immediately before the operation, have been reported recently. When acute plasmapheresis is used in cardiac operations, however, it must be viewed in connection with other techniques for reducing blood consumption such as the Cell Saver (CS) and ultrafiltration devices. In 60 patients undergoing elective aortocoronary bypass grafting, acute plasmapheresis was performed, producing either platelet-poor plasma or platelet-rich plasma, in combination with either the Cell Saver or hemofiltration. Fluid balance during cardiopulmonary bypass was significantly lower in the hemofiltration patients. Postoperatively, none of these patients received donor blood, whereas 4 patients of the Cell-Saver groups needed packed red blood cells. AT-III, fibrinogen, the number of platelets, albumin, total protein, and colloid osmotic pressure were less compromised when hemofiltration was used in combination with acute plasmapheresis in contrast to combination with the Cell-Saver technique. Plasma hemoglobin was without differences during the investigation period, and polymorphonuclear elastase was less increased when platelet-rich plasma was produced preoperatively. On the first postoperative day, most of the differences between the groups had already disappeared. We conclude that when acute plasmapheresis is used in cardiac operations, discarding of plasma by the Cell Saver should be avoided and ultrafiltration devices should replace centrifugation techniques for blood conservation.

(Ann Thorac Surg 1990;50:62–8)

In the face of increasing awareness of the possibility of transmission of viral diseases such as acquired immunodeficiency syndrome, reducing blood loss and minimizing the need for homologous blood transfusion in cardiac surgery are obvious necessities [1, 2]. Furthermore, homologous blood is not an unlimited resource and, particularly in patients with rare blood groups, donor blood might run short [3]. Many approaches to blood conservation are available in cardiac surgery, including nonhemic priming of the extracorporeal circuit, acute normovolemic hemodilution, use of red blood cell recovery devices, and administration of drugs [1, 3, 4]. Use of the Cell Saver (CS) is now the most popular technique to concentrate blood during cardiopulmonary bypass (CPB) and to salvage blood remaining in the circuit after termination of CPB [5]. Ultrafiltration devices are of increasing interest for blood conservation in cardiac surgery owing to the salvage of plasma, in contrast to the CS technique [6–9].

Another method to avoid coagulation abnormalities occurring in conjunction with CPB that reduces requirements of donor blood and blood derivatives appears to be preoperatively performed acute plasmapheresis (APP) [10–12]. By this method, autologous plasma is produced before the start of the operation, preserved from the negative effects of extracorporeal circulation, and retransfused after termination of CPB. Few experiences with this technique are yet available, however, particularly when it is used in combination with other blood conservation methods.

In the present study, the effects of APP used in combination with the CS technique or ultrafiltration devices were investigated with regard to coagulation, blood loss, and donor blood requirements in patients undergoing cardiac operations.

Material and Methods

Patients and Grouping

Sixty male patients scheduled for elective aortocoronary bypass operations were studied. Excluding criteria were a severely depressed myocardial function (left ventricular ejection fraction < 50%; left ventricular end-diastolic pressure > 20 mm Hg), metabolic disorders, and preoperative coagulation abnormalities. The patients were studied consecutively and allocated at random to four groups after informed consent had been obtained according to the protocol of the Institutional Ethic Committee.

GROUP 1 ($n = 15$): Acute plasmapheresis was performed after induction of anesthesia but before onset of operation. Twelve milliliters per kilogram of platelet-poor

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plasma (PPP; centrifugation speed, 5,650 rpm) were withdrawn through a 14-gauge cannula using a PCS 50 system (Haemonetics, Munich, FRG) [10, 11]; the same amount of high-molecular-weight hydroxyethyl starch solution (6% hydroxyethyl starch 450,000/0.7) was infused for volume replacement. Within 20 minutes after CPB was started, the perfusate of the circuit was concentrated by a centrifugation technique (Cell Saver IV, Haemonetics, Munich, FRG). After termination of CPB, blood remaining in the oxygenator and the auxiliary equipment was concentrated and washed. Thus, a concentrate of washed red blood cells was harvested and retransfused until the end of the operation, together with the autologous plasma produced by APP (PPP-CS group).

GROUP 2 (n = 15): Acute plasmapheresis was performed in the same way, but an ultrafiltration device (hemofilter [HF]-60, Fresenius, Oberursel, FRG) was used for blood concentration during and after CPB as described previously [10] (PPP-HF-group).

GROUP 3 (n = 15): Acute plasmapheresis was performed using the same PCS 50 system, but the centrifugation speed was 4,200 rpm to produce a platelet-rich plasma (PRP). The CS technique was used during as well as after CPB as described previously (PRP-CS group).

GROUP 4 (n = 15): Acute plasmapheresis producing PRP was used before start of operation, followed by blood concentration with HF during and after bypass (PRP-HF group).

Anesthesia and Cardiopulmonary Bypass

All patients were premedicated 1.5 hours before induction of anesthesia (morphine sulfate, flunitrazepam). Induction and maintenance of anesthesia was standardized and comparable for all patients, consisting of weight-related dosages of fentanyl, midazolam, and pancuronium bromide.

Before CPB was initiated, anticoagulation was achieved by administration of 300 IU/kg of heparin. Cardiopulmonary bypass was performed with membrane oxygenators (Sorin 41, Sorin, Turin, Italy) with a nonpulsatile flow of 2.4 L/min · m^2; patients' temperature was maintained at almost normothermia (lowest rectal temperature, 34.0° ± 0.3°C). The circuit consisted of 2,200 mL of crystalloids and 250 mL of plasma protein solution (5%). One thousand milliliters of ice-cold Bretschneider's cardioplegia was used initially for myocardial preservation followed by an additional 200 mL every 20 minutes; the operation was performed in "partial" bypass using a monoatrial cannulation technique (two-stage cannula). This technique implies that all fluids are returned to the extracorporeal circuit. Within 30 minutes after start of CPB, the perfusate was concentrated by use of either a centrifugation technique (Cell Saver IV) or an ultrafiltrate device (HF-60) in all patients. The aim was to eliminate 1,000 mL of fluid from the circuit (additional cardioplegic solution).

To maintain the filling volume of the heart-lung machine, Ringer's solution was added when necessary; packed red blood cells were administered when hemoglobin concentration was less than 7 g/dL. All patients were operated on by the same surgical team. Heparin was neutralized with protamine sulfate in a ratio of 1:1.

After termination of CPB, Ringer's solution was administered when pulmonary capillary wedge pressure was less than 8 mm Hg to maintain cardiocirculatory stability. Packed red blood cells were administered when hemoglobin concentration was less than 10 g/dL postoperatively.

Data Points and Measured Variables

Arterial blood samples were taken before the start of APP, at the end of APP, 30 minutes after the start of CPB (after the hemoconcentration procedure ended), immediately after termination of bypass (5 minutes after CPB and before administration of protamine sulfate), at the end of the operation (45 minutes after termination of CPB, after retransfusion of PPP or PRP and the concentrated volume of the circuit [CS blood or HF blood]), 5 hours after termination of CPB, and on the morning of the first postoperative day.

The following variables were measured: hemoglobin, hematocrit, number of platelets, fibrinogen level, AT-III level, heparin plasma concentration, amount of free hemoglobin (plasma hemoglobin), polymorphonuclear elastase level, global coagulation variables (thrombin time, prothrombin time, partial thromboplastin time, thrombelastogram, activated clotting time), colloid osmotic pressure (Sartorius membrane, 20,000 daltons), albumin level, amount of total protein, and blood gas analyses (oxygen tension/inspired oxygen fraction). Fluid balances (calculation of urine/blood output and volume administration), blood loss, and use of Ringer's solution, blood, and blood products, as well as duration until extubation, were documented.

Statistics

Mean values as well as standard deviation were calculated for each variable at each data point. Multiple testing of 1- and 2-factorial analyses of variance followed by Scheffé tests were used for statistical interpretation; p values less than 0.05 were considered significant.

Results

The four groups did not differ with regard to biometric data, preoperative myocardial function, and duration of bypass (Table 1). Acute plasmapheresis lasted from 35.5 to 45.5 minutes without differences between the groups.

Fluid balance during CPB was significantly higher in both CS groups. Postoperative blood loss as well as volume administration also were always more pronounced in these patients, without being statistically significant. None of the HF patients received donor blood or derivatives, whereas 4 patients in the other groups required packed red cells (Table 1). Laboratory results are shown in Table 2.

At the end of the operation, the number of platelets was significantly higher in both HF groups, particularly when PRP was produced by APP (PRP-HF patients). In this

Table 1. Biometric Data and Data on Cardiopulmonary Bypass Blood Loss, Postoperative Blood Loss, and Time Between End of Operation and Extubation[a]

Variable	PPP-CS	PPP-HF	PRP-CS	PRP-HF
Age (yr)	61.0 ± 4.0	59.1 ± 5.7	59.0 ± 3.0	62.7 ± 9.0
Weight (kg)	75.1 ± 3.8	76.3 ± 3.8	78.0 ± 6.0	73.7 ± 8.0
Height (cm)	173.2 ± 5.5	173.0 ± 3.9	168.2 ± 5.8	171.7 ± 8.0
LVEF (%)	65.7 ± 3.8	65.6 ± 5.6	62.9 ± 3.8	62.9 ± 4.4
LVEDP (mm Hg)	15.5 ± 2.2	12.7 ± 3.8	14.6 ± 4.0	16.5 ± 4.0
CPB (min)	80.3 ± 8.8	88.3 ± 8.9	79.2 ± 8.9	88.0 ± 9.8
Ischemia (min)	45.0 ± 4.1	52.8 ± 9.0	46.8 ± 5.0	48.5 ± 7.8
Fluid balance during CPB (mL/kg · min)	0.13 ± 0.02[b]	0.06 ± 0.01	0.14 ± 0.02[b]	0.04 ± 0.01
Blood loss (mL)				
Operation day	310 ± 120	310 ± 140	340 ± 170	235 ± 140
First postoperative day	600 ± 130	530 ± 190	510 ± 190	450 ± 210
Packed RBCs (patients/number)	2/1	0/0	2/1	0/0
Extubation (min)	765 ± 205	795 ± 155	780 ± 210	725 ± 205

[a] Data are shown as mean ± standard deviation. [b] Different from HF patients ($p < 0.001$).

CPB = cardiopulmonary bypass; CS = Cell Saver; HF = hemofiltration; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; PPP = platelet-poor plasma; PRP = platelet-rich plasma.

group, the number of platelets was highest even on the first postoperative day.

The decrease in AT-III and fibrinogen plasma concentrations was significantly more pronounced in the CS patients than in the HF group; AT-III level was even lower in the CS groups on the first postoperative day. Thrombin and prothrombin times were not different, whereas partial thromboplastin time was higher postoperatively in the CS groups as compared with both HF groups. Plasma hemoglobin (free hemoglobin) level was not increased by the APP procedure itself and was not significantly different between the HF and CS groups. Polymorphonuclear elastase was also unchanged by APP. Both PPP groups, however, showed higher levels of elastase during and after termination of bypass than patients in whom PRP was withdrawn. Five hours after bypass and on the first postoperative day, elastase no longer differed between the groups.

Colloid osmotic pressure, albumin level, and total protein level were significantly less decreased in the HF patients; no more differences were noted on the first postoperative day. Pulmonary gas exchange (oxygen tension/inspired oxygen fraction) showed no differences during the entire investigation period; and duration until

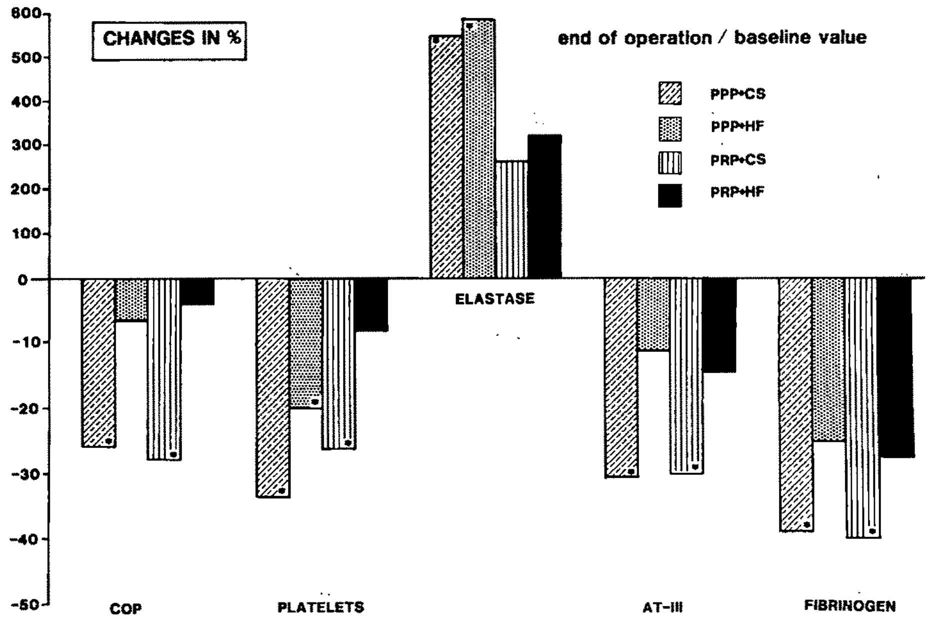

Fig 1. Differences between baseline values and values at the end of the operation (45 minutes after termination of cardiopulmonary bypass) (changes in percentage); * $p < 0.01$. *(COP = colloid osmotic pressure;* CS *= Cell Saver;* HF *= hemofiltration;* PPP *= platelet-poor plasma;* PRP *= platelet-rich plasma.)*

Table 2. Laboratory Variables of the Four Groups[a]

Variable	Group	Before APP	After APP	30-min of CPB	After CPB			First Postop Day
					5 min	45 min	5 h	
Hgb (g/dL)	PPP + CS	13.9 ± 0.5	13.5 ± 0.7	9.1 ± 0.9	12.0 ± 1.0	12.0 ± 1.2	12.5 ± 1.0	11.9 ± 1.0
	PPP + HF	13.8 ± 0.6	13.2 ± 1.0	8.4 ± 0.9	12.2 ± 0.7	12.1 ± 1.1	12.8 ± 1.0	12.0 ± 1.0
	PRP + CS	13.5 ± 0.7	13.1 ± 0.5	8.9 ± 0.8	11.5 ± 0.9	12.2 ± 0.8	12.3 ± 1.1	12.7 ± 1.2
	PPP + HF	13.4 ± 0.6	13.1 ± 0.7	8.9 ± 0.5	12.4 ± 0.5	11.9 ± 1.1	12.7 ± 0.9	12.0 ± 1.1
Platelets (10^3/mL)	PPP + CS	193 ± 37	179 ± 40	146 ± 33^{b}	146 ± 34	133 ± 28^{b}	152 ± 25	154 ± 23
	PPP + HF	207 ± 46	200 ± 34	163 ± 33	151 ± 36	169 ± 26	157 ± 48	172 ± 48
	PRP + CS	202 ± 30	193 ± 40	138 ± 22^{b}	150 ± 28	149 ± 30^{b}	177 ± 31^{b}	190 ± 39^{b}
	PRP + HF	203 ± 41	174 ± 34	169 ± 33	162 ± 41	188 ± 32^{c}	199 ± 33^{c}	209 ± 39^{b}
Free Hgb (mg/dL) (normal, <40)	PPP + CS	22.4 ± 9.0	28.9 ± 6.9	49.9 ± 22.8	66.9 ± 20.1	34.3 ± 16.8	30.5 ± 15.8	33.7 ± 12.0
	PPP + HF	30.5 ± 6.9	34.8 ± 9.8	55.2 ± 23.8	69.2 ± 22.0	38.9 ± 17.9	28.3 ± 14.0	30.4 ± 14.7
	PRP + CS	26.8 ± 8.0	34.2 ± 7.7	60.4 ± 27.9	66.4 ± 19.4	33.6 ± 20.5	34.4 ± 15.0	31.1 ± 18.9
	PRP + HF	24.3 ± 9.2	28.9 ± 3.9	59.8 ± 30.0	78.8 ± 20.4	37.8 ± 23.7	33.3 ± 20.3	28.7 ± 17.9
Elastase (μg/L) (normal, 80–130)	PPP + CS	64 ± 33	70 ± 30	401 ± 102	477 ± 200^{d}	422 ± 103^{d}	289 ± 100	277 ± 99
	PPP + HF	70 ± 17	76 ± 30	309 ± 102	468 ± 144^{d}	407 ± 106^{d}	301 ± 102	301 ± 78
	PRP + CS	90 ± 22	89 ± 33	211 ± 88	260 ± 88	255 ± 100	240 ± 67	241 ± 77
	PRP + HF	92 ± 33	79 ± 40	250 ± 85	286 ± 139	301 ± 109	325 ± 85	246 ± 60
Heparin (IU/mL)	PPP + CS	1.30 ± 0.3	1.20 ± 0.4	17.2 ± 2.4	14.0 ± 2.2	1.22 ± 0.3	1.44 ± 0.3	2.50 ± 0.6
	PPP + HF	1.55 ± 0.3	1.67 ± 0.3	16.3 ± 3.0	10.5 ± 2.3	1.67 ± 0.4	1.79 ± 0.5	2.03 ± 0.6
	PRP + CS	1.33 ± 0.2	1.40 ± 0.3	16.2 ± 2.2	12.3 ± 2.0	1.30 ± 0.3	1.49 ± 0.4	2.66 ± 0.7
	PRP + HF	1.56 ± 0.5	1.38 ± 0.4	17.7 ± 1.9	11.7 ± 1.7	1.44 ± 0.3	1.75 ± 0.6	2.02 ± 0.4
AT-III (%) (normal, 80–120)	PPP + CS	122 ± 15	111 ± 12	67 ± 19	65 ± 20^{e}	85 ± 18^{e}	99 ± 22^{e}	98 ± 23^{e}
	PPP + HF	123 ± 13	113 ± 17	76 ± 20	80 ± 21	109 ± 12	126 ± 21	118 ± 23
	PRP + CS	122 ± 11	100 ± 16	64 ± 13	68 ± 13^{e}	86 ± 18^{e}	100 ± 20^{e}	101 ± 21^{e}
	PRP + HF	119 ± 18	99 ± 14	79 ± 17	74 ± 15	101 ± 16	119 ± 11	122 ± 12
Fibrinogen (g/L) (normal, 1.5–4.5)	PPP + CS	3.67 ± 0.5	3.44 ± 0.5	1.57 ± 0.4^{e}	1.71 ± 0.5^{e}	2.24 ± 0.6^{e}	2.70 ± 0.8	3.63 ± 0.7
	PPP + HF	3.41 ± 0.7	3.20 ± 0.7	1.90 ± 0.4	1.85 ± 0.6	2.88 ± 0.5	3.12 ± 0.6	3.79 ± 0.6
	PRP + CS	3.40 ± 0.7	3.00 ± 0.3	1.60 ± 0.5^{e}	1.50 ± 0.4^{e}	2.06 ± 0.4^{e}	2.70 ± 0.5	3.88 ± 0.6
	PRP + HF	3.69 ± 0.6	3.02 ± 0.6	1.91 ± 0.3	1.88 ± 0.4	2.96 ± 0.3	2.99 ± 0.3	3.78 ± 0.6
Thrombin time (s) (normal, 16–22)	PPP + CS	17.0 ± 2.8	22.0 ± 5.0	. . .	. . .	20.1 ± 3.0	18.5 ± 4.6	19.9 ± 3.0
	PPP + HF	19.7 ± 3.3	22.6 ± 4.4	. . .	. . .	23.8 ± 5.0	20.7 ± 3.0	22.8 ± 4.0
	PRP + CS	18.9 ± 2.0	19.8 ± 4.4	. . .	. . .	24.7 ± 4.0	21.9 ± 3.3	24.9 ± 5.0
	PRP + HF	18.5 ± 3.0	19.3 ± 3.3	. . .	. . .	27.3 ± 4.9	23.1 ± 6.1	19.1 ± 2.7
Prothrombin time (%) (normal, 70–120)	PPP + CS	75.8 ± 12	77.6 ± 13	. . .	. . .	40.6 ± 9.9	62.1 ± 9.0	65.9 ± 13
	PPP + HF	74.9 ± 12	80.7 ± 17	. . .	. . .	34.8 ± 9.0	69.0 ± 11	65.9 ± 12
	PRP + CS	78.9 ± 13	70.8 ± 12	. . .	. . .	38.0 ± 7.8	66.9 ± 7.9	72.0 ± 16
	PRP + HF	83.0 ± 17	74.0 ± 13	. . .	. . .	57.9 ± 12	80.9 ± 13	81.9 ± 13
Partial thromboplastin time (s) (normal, 30–40)	PPP + CS	40.9 ± 3.9	46.0 ± 2.2	. . .	. . .	67.0 ± 13	50.7 ± 6.1^{e}	70.0 ± 8.8^{e}
	PPP + HF	45.0 ± 3.3	40.1 ± 2.9	. . .	. . .	66.2 ± 16	34.1 ± 6.0	54.9 ± 3.3
	PRP + CS	43.0 ± 3.4	46.9 ± 3.0	. . .	. . .	71.0 ± 19	52.6 ± 4.9^{e}	66.9 ± 7.0^{e}
	PRP + HF	44.0 ± 4.8	48.0 ± 3.1	. . .	. . .	65.9 ± 20	27.6 ± 9.9	28.0 ± 4.2
COP (mm Hg) (normal, 18–22)	PPP + CS	20.0 ± 2.5	20.3 ± 1.9	8.0 ± 1.2^{e}	11.2 ± 1.9	15.9 ± 2.2^{e}	21.0 ± 2.7	21.9 ± 2.0
	PPP + HF	19.8 ± 2.0	19.3 ± 1.6	12.1 ± 1.3	12.5 ± 2.0	18.5 ± 2.0	24.0 ± 2.3	24.5 ± 2.5
	PRP + CS	20.7 ± 1.9	20.1 ± 2.0	9.0 ± 2.1^{e}	11.0 ± 1.9	15.0 ± 2.1^{e}	20.1 ± 1.9	21.1 ± 2.0
	PRP + HF	18.9 ± 1.5	18.4 ± 0.9	12.0 ± 1.5	11.9 ± 0.8	18.0 ± 1.4	22.9 ± 2.1	22.9 ± 1.6
Albumin (g/dL) (normal, 3.4–4.4)	PPP + CS	3.54 ± 0.3	2.80 ± 0.4	1.68 ± 0.3^{e}	2.00 ± 0.4	2.46 ± 0.3^{e}	2.95 ± 0.3^{e}	3.00 ± 0.2
	PPP + HF	3.34 ± 0.2	2.90 ± 0.2	1.98 ± 0.3	2.03 ± 0.2	3.00 ± 0.2	3.33 ± 0.3	3.40 ± 0.2
	PRP + CS	3.62 ± 0.2	2.60 ± 0.2	1.78 ± 0.2^{e}	1.90 ± 0.3	2.45 ± 0.3^{e}	2.86 ± 0.2^{e}	3.03 ± 0.3
	PRP + HF	3.50 ± 0.3	2.55 ± 0.2	2.09 ± 0.2	1.99 ± 0.2	2.99 ± 0.2	3.28 ± 0.3	2.99 ± 0.2

(continued)

Table 2. (Continued)

Variable	Group	Before APP	After APP	30-min of CPB	After CPB 5 min	After CPB 45 min	After CPB 5 h	First Postop Day
Total protein (g/dL) (normal, 5.5–8.0)	PPP + CS	5.98 ± 0.5	4.90 ± 0.5	3.03 ± 0.3^e	3.25 ± 0.4^e	4.12 ± 0.3^e	4.68 ± 0.3^e	4.94 ± 0.5
	PPP + HF	5.78 ± 0.4	5.01 ± 0.4	3.63 ± 0.3	3.88 ± 0.3	5.00 ± 0.4	5.44 ± 0.4	5.89 ± 0.3
	PRP + CS	5.80 ± 0.6	4.50 ± 0.3	3.01 ± 0.3^e	3.01 ± 0.4^e	3.80 ± 0.3^e	4.34 ± 0.3^e	4.80 ± 0.4
	PRP + HF	5.57 ± 0.2	4.57 ± 0.2	3.50 ± 0.2	3.45 ± 0.3	4.65 ± 0.3	5.12 ± 0.2	4.89 ± 0.3
PaO_2/FiO_2 (mm Hg)	PPP + CS	390 ± 55	399 ± 70	244 ± 44	388 ± 101	344 ± 88	360 ± 70	544 ± 133
	PPP + HF	369 ± 59	399 ± 77	233 ± 30	378 ± 70	345 ± 49	427 ± 88	555 ± 84
	PRP + CS	400 ± 66	402 ± 77	230 ± 51	389 ± 99	370 ± 44	440 ± 100	501 ± 123
	PRP + HF	388 ± 81	410 ± 44	210 ± 40	355 ± 40	363 ± 58	398 ± 120	548 ± 141

[a] Data are shown as mean ± standard deviation. [b] Different from HF patients ($p < 0.001$); [c] Different from all patients ($p < 0.01$); [d] Different from PRP patients ($p< 0.01$); [e] Different from HF patients ($p < 0.01$).

APP = acute plasmapheresis; COP = colloid osmotic pressure; CPB = cardiopulmonary bypass; CS = Cell Saver; FiO_2 = inspired oxygen fraction; HF = hemofiltration; Hgb = hemoglobin; PaO_2 = oxygen tension; PPP = platelet-poor plasma; PRP = platelet-rich plasma.

extubation was comparable for all groups as well. Hemoglobin level (Table 2), hematocrit, activated clotting time, thromboelastogram, electrolyte levels, and heparin plasma concentration did not differ significantly between the groups.

Baseline values and values at the end of the operation are shown in Figure 1, demonstrating the most extensive differences between CS and HF patients. In the further course of the study period, particularly on the first postoperative day, most of these differences had already disappeared and values had returned almost to normal in all groups.

None of our patients suffered from sequelae attributable to the study; all patients were discharged from the intensive care unit to a normal ward on the third postoperative day.

Comment

Basic properties of the coagulation system and its response to CPB have been outlined by several investigators [13]. Extracorporeal circulation of blood may lead to alterations in hemostatic balance, which is sometimes the cause of bleeding disorders in cardiac surgery [14].

Plasma preparations such as fresh-frozen plasma and platelets are often used during extracorporeal circulation with the aim of replacing both the oncotic power and the water-retaining capacity of the proteins as well as correcting coagulation disturbances [3]. However, this is also associated with the risk of transmitting viral diseases and other adverse effects [2, 15, 16]. Autologous plasma has been produced in elective orthopedic patients using plasmapheresis performed weeks or even months before the operation [17]. A significant reduction in blood consumption was achieved with this technique in these patients.

Preoperatively performed APP might add a new dimension to perioperative efforts to reduce blood loss, limit blood bank usage, and optimize the coagulation system in cardiac surgery patients, as has been described recently [10, 11]. Acute plasmapheresis can be used immediately before operation even in patients in whom acute hemodilution is not possible because of reduced hemoglobin values. There is no risk of reducing oxygen transport capacity in patients with limited coronary artery reserve, such as patients undergoing coronary operations [18].

Use of blood concentration devices such as the CS has proved a progressive measure toward reduction of postoperative donor blood in cardiac surgery [5]. Ultrafiltration, on the other hand, differs substantially from this centrifugation technique, removing only excess fluid from the blood while completely preserving plasma proteins that are discarded by the CS technique. Thus, salvage of the plasma fraction appears to be of interest, particularly in patients in whom autologous plasma is removed preoperatively by APP.

As demonstrated in our study, the ability to return elements of plasma fraction provides advantages by optimizing the coagulation system and by improving colloid osmotic pressure. Albumin and total protein levels were reduced significantly by APP, whereas colloid osmotic pressure remained almost unchanged owing to the colloid osmotic pressure of the high-molecular-weight hydroxyethyl starch solution. During CPB as well as at the end of the operation, colloid osmotic pressure was at a higher level in the HF patients as compared with the CS groups. According to Starling's equation, this contributes to maintenance of optimal pulmonary fluid hemostasis [19–21] and pulmonary function.

With regard to number of platelets, fibrinogen level, and AT-III plasma concentration, HF was shown to be superior to CS technique in this study: HF affected these variables less than the CS system by preserving the plasma fraction. Production of autologous PRP in combination with HF resulted in the highest number of platelets during and after CPB. This is of importance because hematological and coagulation abnormalities sometimes complicate CPB [13]. Three major objections must be considered, however: (1) possible clearance of heparin by the hemofilter; (2) activation of various deleterious humoral cascades [22–24], resulting in cellular damage from APP or the hemofilter itself, and less removal of these "toxic" products by the HF technique; and (3) additional blood traumatization by APP and a less effective removal of plasma hemoglobin by HF.

First, heparin concentrations were not different between the groups during the entire investigation period. Second, the level of elastase, the most remarkable proteolytic enzyme released by polymorphonuclear neutrophils, was not increased by APP itself and did not differ between the CS or HF patients in the further course of investigation. Elastase plasma concentration in all APP patients was not as high as reported by other investigators in comparable study protocols [26] or even in patients with shock or sepsis with polymorphonuclear elastase values greater than 2,000 μg/L [27]. Elastase plasma concentration was lowest in the PRP patients, indicating a possible important feature of the APP procedure in cardiac surgery.

Last but not least, the level of plasma hemoglobin (free hemoglobin) was not significantly different between the groups. Free hemoglobin values in our investigation were comparable with findings of other investigators using no ultrafiltration device [28]. The importance of slightly increased plasma hemoglobin values is often exaggerated; free hemoglobin is often increased even after physical training and the clearance rate is very high. None of our patients suffered from any organ failure; in particular, renal and pulmonary function were within normal range in all patients (ie, pulmonary gas exchange and duration until extubation were without differences between the groups).

In this study in rather healthy patients undergoing cardiac operations, we showed the advantages of using HF in combination with APP in comparison with use of the CS system together with APP. The coagulation system and the colloid osmotic pressure tended to normalize earlier in HF-treated patients. None of the HF patients needed donor blood; however, the differences with the CS groups, in which homologous blood was transfused (4 of 30 patients), were statistically not significant, most likely owing to the small number of patients studied. Thus, this combined technique for blood conservation should be tested in larger clinical trials.

One aspect that should not be neglected when using blood conservation techniques is the costs, although it is difficult to discuss this aspect owing to the very different medical systems that exist in different countries. Fresh-frozen plasma is approximately twice as expensive as autologous plasma, and platelets are approximately six times more expensive than PRP produced by APP. The HF technique is substantially less expensive than the CS procedure, even more when the discarded plasma is replaced by fresh-frozen plasma. Moreover, consequences of possible transmission of viral diseases by blood products would result in a huge enhancement of cost. We conclude that preoperatively performed APP may be an additional tool in the efforts to reduce homologous blood and blood derivative use in cardiac operations. When APP is used, however, loss of plasma owing to hemoconcentration by the centrifugation technique should be avoided. The beneficial effects of "rescuing" plasma from extracorporeal oxygenation, and retransfusing it thereafter, appears to be blunted by elimination of plasma by the CS. Thus, the CS should be replaced in patients undergoing APP by HF during and after bypass to optimize coagulation as well as colloid osmotic pressure.

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REVIEW OF RECENT BOOKS

General Thoracic Surgery, Third Edition
Edited by Thomas W. Shields
Philadelphia, Lea & Febiger, 1989
1,250 pp, illustrated, $150.00

Reviewed by Blair A. Keagy, MD

The book *General Thoracic Surgery*, edited by Thomas Shields, belongs on the shelf of every general thoracic surgeon. The recently published third edition is larger (178 more pages and 25 additional chapters) than its predecessor published in 1983 and has been substantially updated to include the latest information on diagnosis and treatment of thoracic surgical problems. Analyses of the newest radiological techniques are available as well as reports on therapeutic advances in adjuvant therapy and descriptions of new surgical techniques. The book contains slightly modified versions of its classic chapters. The outstanding "Tracheal anatomy and surgical approach" section by Grillo has been retained, while the pulmonary resection chapter has been changed to emphasize the more frequent use of staplers. New chapters addressing sleeve lobectomy and pneumonectomy, as well as the median sternotomy approach to pulmonary resection, are welcome additions. There is up-to-date information on combined therapy (chemotherapy, radiotherapy, immunotherapy) in both esophageal cancer and pulmonary malignancies. Other new sections include free intestinal transfer and microvascular techniques used with lesions of the esophagus, as well as new chapters on adult respiratory distress syndrome and lung transplantation. In summary, an outstanding book has been made even better. The illustrations are good, the narrative sections are clear and concise, and the book is well organized. I used the book frequently in my clinical practice during this evaluation and can give it my highest recommendation.

Chapel Hill, North Carolina

Late Results of Aortic Valvotomy for Congenital Valvar Aortic Stenosis

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Fifty-one patients, aged 1 to 18 years, having aortic valvotomy for congenital valvar aortic stenosis between 1956 and 1986 were followed up. The average age at operation was 11.5 years, with an operative mortality of 3.9%. The aortic valve gradient decreased from a mean preoperative value of 91 mm Hg to 27 mm Hg postoperatively. Current follow-up was 90% and averaged 16.8 years. Late cardiac mortality was 17.6%, with actuarial survival of 93.7% at 10 and 15 years, 81.8% at 20 and 25 years, and 70.9% at 28 years. Nineteen patients required reoperation (39%) at a mean of 17.7 years postoperatively, with a reoperation-free survival of 98% at 10 years. The reoperation rate accelerated in the following decade to 3.3% per year. Ten patients without reoperation were evaluated by continuous-wave Doppler echocardiography. The mean gradient was 21.6 mm Hg, and 90% had mild to moderate aortic insufficiency. This study confirms the efficacy of valvotomy in this age group and suggests that long-term survival and time to reoperation may be longer than previously reported.

(Ann Thorac Surg 1990;50:69–73)

Congenital valvar aortic stenosis refers to obstruction of the left ventricular outflow tract at the annular level owing to imperfect cusp development. It represents 5% of all congenital heart disease [1, 2]. Aortic valvotomy under direct vision was first described in 1956 [3, 4] using hypothermia and shortly thereafter using cardiopulmonary bypass [5, 6]. It remains the preferred operation for this disease in young patients. It is commonly accepted that aortic valvotomy is a palliative operation that provides initial benefit and decreased risk of sudden death but is followed by an increasing incidence of reoperation, return of symptoms, and late death. Most reported series conclude that all patients treated with valvotomy will ultimately require aortic valve replacement [7–11], and two groups of investigators [12, 13] state that all patients will need reoperation within 20 years. The purpose of this study was to determine the long-term benefit of aortic valvotomy in the treatment of congenital valvar aortic stenosis in terms of incidence of reoperation and sudden death without reoperation.

Material and Methods

All patients with isolated congenital valvar aortic stenosis who had aortic valvotomy at the National Institutes of Health (NIH) between 1956 and 1986 were considered for this study. Newborns and infants aged less than 1 year were not included because none were referred to the NIH. Patients aged more than 18 years were excluded. Fifty-one patients satisfied these criteria. The average age at the time of operation was 11.5 years (range, 1 to 18 years). There were 37 (73%) male and 14 (27%) female patients. All patients underwent preoperative cardiac catheterization and were asked to return 6 to 12 months after operation to quantitate any residual postoperative stenosis or insufficiency. Forty-three patients (88%) had cardiac catheterization during this interval.

Indications for operation included a peak systolic aortic valve gradient greater than 50 mm Hg measured by cardiac catheterization, the presence of symptoms (angina, syncope, dyspnea on exertion, or fatigue), or both. Fifty patients (98%) had gradients in excess of 50 mm Hg, and in 33 (66%) symptoms were manifest. One patient had the operation for symptoms alone, whereas the sole indication in 17 (33%) was the presence of a gradient. Each patient underwent open aortic valvotomy using cardiopulmonary bypass with either moderate hypothermia or standard cardioplegic techniques. Thirty-seven valves (73%) were bicuspid, and the remainder were tricuspid. None was unicuspid, and one valve was not described because the procedure was performed by the transventricular approach.

A diligent search was performed to contact each patient or a family member. Those without a subsequent operation were reevaluated by thorough physical examination, chest roentgenogram, electrocardiogram, and echocardiogram with continuous-wave Doppler echocardiography. Patients unable to return to the NIH were evaluated by their local physician. Functional class was assigned according to the New York Heart Association criteria [14]. Left ventricular hypertrophy was assessed by electrocardiogram using the criteria established by Romhilt and Estes [15]. Cardiomegaly was reported if the cardiothoracic ratio, as measured by posteroanterior chest roent-

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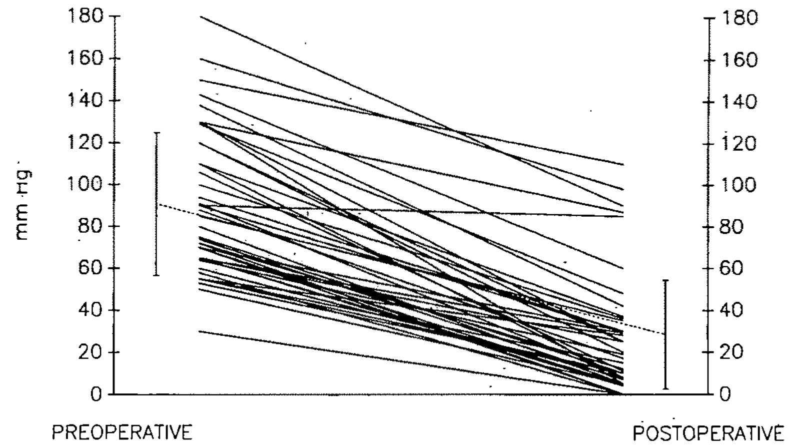

Fig 1. Reduction in peak systolic aortic valve gradient (in millimeters of mercury) as measured by cardiac catheterization. Forty-three patients had both preoperative and postoperative evaluation.

genogram, was greater than or equal to 0.5. Aortic valve gradients were measured by continuous-wave Doppler echocardiography.

Mortality was defined in terms of operative and late deaths. Operative death occurred within 30 days of valvotomy or during hospitalization. Death after discharge was classified as late according to the guidelines of The Society of Thoracic Surgeons [16, 17]. Late deaths were described as being related or unrelated to cardiac causes. Actuarial analysis of long-term survival used standard techniques [18, 19] and the Statistical Analysis Systems (Statistical Analysis Systems Institute, Cary, NC). Probability estimates, expressed as the standard error of the mean, used BMDP Statistical Software (University of California, Los Angeles, CA).

Results

Forty-nine patients survived aortic valvotomy, for an operative mortality of 3.9%. The only operative deaths occurred in 1957 and 1958. The first resulted from congestive heart failure two hours after operation secondary to iatrogenic aortic insufficiency, and the second from ventricular fibrillation 12 hours into the postoperative period. Since 1959, all patients have survived the procedure.

A comparison of preoperative and postoperative catheterization documented a substantial reduction (74% ± 3%) of the peak systolic aortic valve gradient from a mean of 91 ± 5.2 to 27 ± 4.3 mm Hg (Fig 1). Six patients (14%) had postoperative gradients greater than 50 mm Hg. The mean follow-up for this subset was 14.7 years. Four patients required subsequent aortic valve replacement at a mean interval of 15.5 years, and 2 died secondary to cardiac dysrrhythmia at 19.6 and 21 years, respectively. Aortic insufficiency was absent in all patients before valvotomy; however, 7 patients (16.3%) had documented insufficiency on postoperative catheterization.

Survivors and nonsurvivors were compared with respect to the presence of a bicuspid valve and the magnitude of both preoperative and postoperative aortic valve gradients. The presence of a bicuspid valve did not influence the extent of either preoperative or postoperative gradient significantly ($p > 0.05$). Gradients in survivors did not differ significantly from those in nonsurvivors ($p > 0.05$). Analyses of patients whose follow-up exceeded 20 years showed no significant difference in preoperative or postoperative gradients, number of valve cusps, reoperation-free survival, or mortality. Hence, in this series, neither the presence or absence of a bicuspid valve nor the magnitude of either the preoperative or postoperative gradient predicted the length of postoperative survival.

Forty-four (90%) of the 49 hospital survivors were contacted within the past year. Pertinent available data from those not located during the follow-up interval were used until the time of last contact. For actuarial purposes, follow-up ceased once the patient had reoperation, was lost to follow-up, or died. The mean follow-up was 16.8 years; the longest was 28.5 years, and 16 patients (31%) were followed for more than 20 years. Thirty-eight patients (75%) were alive. Operative mortality accounted for 3.9%, and long-term mortality was 21.6% (13.7% was cardiac related). The most frequent cause of late death in this study was dysrrhythmia (36%) followed by pulmonary embolus (18%), congestive heart failure (9%), myocardial infarction (9%), and motor vehicle accident and suicide (9% each). The cause of death in 1 patient was unknown and, for actuarial purposes, was considered cardiac. Mortality for the 16 patients whose follow-up was longer than 20 years was 6.25%. This was surprisingly low; however, when compared with the remainder of the population there was no significant difference ($p > 0.05$).

Reoperation was performed in 19 patients (39%). The predominant indication was the return of symptoms; ie, angina, syncope, exercise intolerance, or fatigue, and the presence of restenosis (37%) followed by restenosis with insufficiency (16%) or pure insufficiency (16%). Only two patients (11%) required reoperation for asymptomatic restenosis, ie, a peak systolic gradient greater than 50 mm Hg. One patient underwent resuspension of the aortic valve 11 months after valvotomy; the remainder required aortic valve replacement. Only 1 patient required a second valve replacement, which was performed to correct restenosis and a perivalvar leak of a bioprosthesis 4½ years later. The mean time from aortic valvotomy to reoperation was 17.7 years. A bicuspid valve was present in 15 patients (79%) who required reoperation; this did not differ significantly from the initial population ($p > 0.05$).

Actuarial analysis performed on the survivors of initial valvotomy produced two curves (Fig 2). Curve A excluded deaths judged to be noncardiac, whereas curve B included deaths from all causes. Survival was 91.7% at 10 years and 89.3% at 15 years. Twenty- and 25-year survivals were 72.4%; survival at 28 years was 62.7%. With noncardiac deaths excluded (curve A), survival remained 100% at 5 years but, in comparison, both 10- and 15-year survival improved to 93.7%. Twenty- and 25-year survivals were 81.8%; survival at 28 years improved to 79.9%. Seventy-five percent survival increased from 19.3 ± 1.58 years to 26.6 ± 0.57 years.

Reoperation-free survival was 98% at both the 5- and 10-year intervals (Fig 3). Thereafter, survival decreased linearly. Fifteen-year survival was 88.6%, whereas 63.9% and 50.3% of patients avoided reoperation at the 20- and 25-year milestones, respectively. At 28 years, only 43.6% of patients had not had reoperation. The 75% reoperation-free survival interval was 17.7 years.

Thirteen (93%) of the 14 survivors who did not undergo reoperation were evaluated during the past year. Eleven (79%) were examined at the NIH and the remainder were examined by their local physician. Mean follow-up was 19.8 years. All patients were in New York Heart Association functional class I. Seventy percent had cardiomegaly by radiographic measurement; left ventricular hypertrophy (LVH) was apparent on electrocardiogram in 18%, with an additional 27% having probable LVH. Ten patients (71%) had echocardiography and measurement of the aortic valve gradient by continuous-wave Doppler echocardiography. Gradients ranged from 9 to 67 mm Hg (mean, 21.6 mm Hg). Some degree of insufficiency was present in 9 patients (90%) by echocardiography. Insufficiency was interpreted to be absent in 1 patient (10%), mild in 3 (30%), mild to moderate in 3 (30%), moderate in 2 (20%), and severe in 1 (10%). The presence of LVH on electrocardiogram was compared with the degree of stenosis measured by Doppler echocardiography. The only patients with LVH had aortic valve gradients of 34 and 64 mm Hg and had moderate and severe insufficiency, respectively.

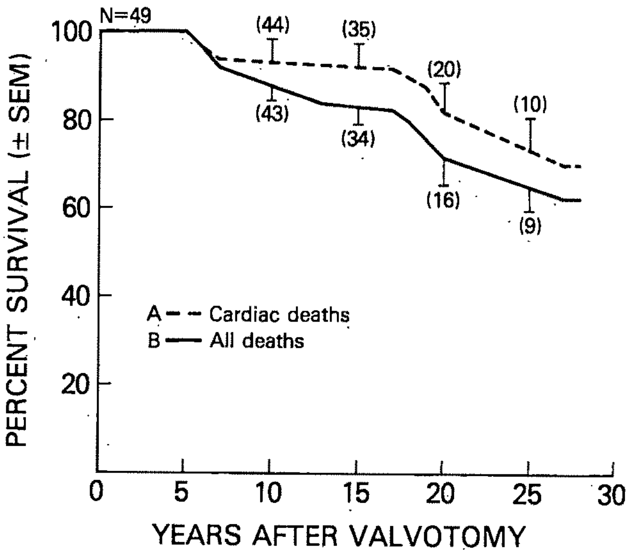

Fig 2. Actuarial analysis of all patients surviving aortic valvotomy for congenital valvar aortic stenosis; curve A excludes noncardiac deaths and curve B includes all causes of death. (N = number of patients at risk; SEM = standard error of the mean.)

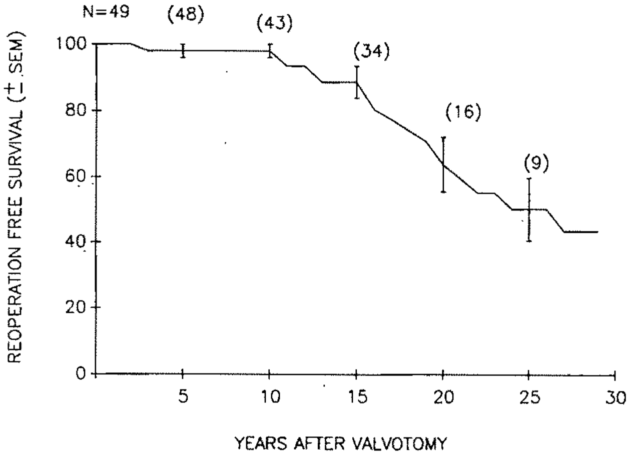

Fig 3. Actuarial analysis of operation-free survival in percentage of all patients surviving aortic valvotomy for congenital aortic stenosis. (N = number of patients at risk; SEM = standard error of the mean.)

Comment

Aortic valvotomy has an appreciably higher mortality when performed in neonates and somewhat higher when performed in infants [2,23–25] because they have a more severe form of the disease. Most neonates and young infants come to operation critically ill and may have associated left-sided congenital anomalies such as left ventricular hypoplasia, endocardial fibroelastosis, congenital mitral stenosis, coarctation of the aorta, or ventricular septal defect, which are not amenable to valvotomy alone. Fortunately, for patients aged 1 year or older, as demonstrated by this study, aortic valvotomy is a low-risk procedure [2, 24]. Published mortality data for patients aged more than 1 year vary from 0% to 15.7% (average, 2.8%) [22]. The operative mortality in this series was 3.9%. This is slightly higher than that of several studies [9, 11, 27, 29] but reflects the historical nature of this population. The absence of operative deaths in 49 patients at the NIH for the past 27 years reflects the current safety of aortic valvotomy.

Late mortality remains somewhat higher. Long-term survival was 74% in this population, with a cardiac-related mortality of 14%. This agrees with the 13% reported by Hossack and colleagues [29], and is slightly better than the 18.5% reported by Stewart and associates [7] and the 22% reported by Hsieh and co-workers [8], which are the only other studies to date with mean follow-up exceeding 15 years. These studies, considered in the aggregate, suggest that the overall long-term mortality is slightly greater than 1% per year. Mortality from

Table 1. Outcome of Patients With Postoperative Aortic Insufficiency on Cardiac Catheterization

NYHA functional class I	2
Aortic valve replacement	1
Died	4
Pulmonary embolus	2
Dysrrhythmia	1
Myocardial infarction	1
Total	7

NYHA = New York Heart Association.

the present study was absent in the first 5 years after valvotomy and then increased to approximately 1.5% per year.

Catheterization data in this series attest to the efficacy of aortic valvotomy in relieving left ventricular outflow tract obstruction and confirm previous reports [20–22]. However, 14% of patients had residual gradients of 50 mm Hg or greater. Two thirds required aortic valve replacement, and the remaining third died of dysrrhythmias. Patients with residual gradients of this magnitude should be considered at high risk of sudden death and require close follow-up. Reoperation should be considered earlier in these patients with residual stenosis.

Insufficiency was present in 16.2% who had postoperative cardiac catheterization. This agrees with the 21% quoted by Mackworth-Young and colleagues [27], and reaffirms the prevalence of this complication. Mild insufficiency has not been considered to affect long-term survival adversely; however, patients with postoperative aortic insufficiency in this series had a disproportionate number of late deaths (57%); 28.6% of the deaths were cardiac in nature (Table 1). Although not statistically significant in this small population, aortic insufficiency may adversely affect the outcome of aortic valvotomy; until this possibility can be refuted, more attentive follow-up of these patients is warranted.

The prospect of reoperation, usually requiring aortic valve replacement, emphasizes the palliative nature of aortic valvotomy. In this series, 19 patients (39%) required reoperation. Indications included recurrent stenosis, symptoms, or aortic insufficiency. The incidence of reoperation closely compares with reports of 38% by Stewart and associates [7], 33% by Hossack and colleagues [29], and 36% by Hsieh and co-workers [8], whose follow-up averaged 15, 13, and 17.7 years, respectively. The average time to reoperation in the present study was 17.7 years and by life-table analysis 50% of patients would be expected to require reoperation 26 years after initial valvotomy.

In this series, the likelihood of subsequent operation after valvotomy was approximately 2% over the entire first decade, or 0.2% per year (Fig 3). Thereafter, the risk of reoperation increased significantly and continued linearly at 3.3% per year. Assuming that this risk remains linear, all patients would be reoperated on within 40 years. These data do not agree with those of Presbitero and colleagues [13] and Sommerville and co-workers [12], and suggest that reoperation-free survival may be longer than previously reported. In addition, the low rate of reoperation in the first decade and the dramatic increase in the second corroborate the findings of Lawson and associates [26] and Presbitero and colleagues [13]. Although the prospect of almost a decade free from reoperation and the possibility of deferring valve replacement for up to 40 years are encouraging, these data reiterate the palliative nature of aortic valvotomy and the inevitability of reoperation.

Echocardiographic and Doppler echocardiographic data from patients who have had aortic valvotomy for congenital aortic stenosis and whose average follow-up was 20 years showed a mean estimated gradient of 22 mm Hg. Almost half of these values were within 15 mm Hg of the gradient measured at postoperative cardiac catheterization. Only 1 patient's gradient was greater than 40 mm Hg; this patient also had severe aortic insufficiency and LVH. Although this population was small, the finding of LVH on electrocardiogram was present only in patients whose gradient exceeded 30 mm Hg and who had moderate to severe aortic insufficiency.

Although aortic insufficiency is present in about one fifth of patients 6 to 12 months after operation, these data suggest that insufficiency progresses with time. Even though this cohort was asymptomatic about 20 years later, 50% had moderate to severe insufficiency and 90% had some insufficiency detectable by Doppler echocardiography. Thus, asymptomatic aortic insufficiency may be more prevalent and serious than currently believed, and the presence of LVH on electrocardiogram suggests serious aortic stenosis with at least moderate insufficiency. Finally, despite the limitations of continuous-wave Doppler echocardiography, these results confirm the excellent relief of left ventricular outflow tract obstruction afforded by aortic valvotomy and demonstrate the usefulness of noninvasive modalities in identifying stenosis and insufficiency.

Conclusion

Aortic valvotomy remains an excellent palliative procedure for congenital aortic stenosis. Operative mortality is low in children, adolescents, and adults, and relief of left ventricular outflow tract obstruction is substantial and predictable. Neonates and infants (not included in this study), however, have a more severe form of the disease and operative mortality is still substantial. The present study reaffirms the effectiveness of valvotomy in decreasing the risk of early sudden death and suggests that long-term survival is also improved. Mortality is virtually absent for the first 5 years after valvotomy and then averages 1.5% per year. Furthermore, the need for reoperation is unlikely during the first decade but increases linearly at 3.3% per year thereafter. Although only 39% of patients required reoperation, it is estimated that all patients will require reoperation within 40 years of the initial procedure.

Postoperative insufficiency is a real, yet understandable, imperfection of aortic valvotomy. It occurs almost 20% of the time and may indicate a poorer prognosis. Although not firmly established by this study, the considerable number of late deaths in this group suggest that patients with postoperative insufficiency require more attentive long-term follow-up. Similarly, postoperative gradients of 50 mm Hg or greater predispose patients to sudden death and earlier aortic valve replacement. Hence, annual noninvasive testing is recommended for patients with either residual stenosis or postoperative insufficiency.

All patients without reoperation since initial valvotomy were asymptomatic. Echocardiographic and continuous-wave Doppler echocardiographic data confirmed the excellent long-term relief of stenosis afforded by open valvotomy and illustrated the gradual restenosis and progression of aortic insufficiency. Evidence of LVH on electrocardiogram was present only in patients with aortic valve gradients greater than 30 mm Hg and moderate to severe insufficiency. Hence, LVH may be a strong indicator of restenosis with, at least, moderate aortic insufficiency. Cardiomegaly, as determined by chest roentgenogram, was a common finding, present in 70% of patients.

Finally, the low operative mortality and the excellent long-term relief of stenosis and symptoms provided by open aortic valvotomy in patients aged more than 1 year of age establish it as the standard procedure with which balloon valvoplasty and other future nonoperative therapies for congenital aortic stenosis should be compared.

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Sutureless Ring Graft Replacement of Ascending Aorta and Aortic Arch

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Complications after aortic replacement that result from prolonged graft insertion time and technical difficulties with suturing through friable, diseased aortic tissue can be addressed with use of the sutureless intraluminal ring graft. Between 1978 and 1989, we replaced the ascending aorta or aortic arch with this device in 49 patients. At no time were we unable to use a sutureless graft during a procedure. Twenty-eight cases of aneurysmal disease and 21 cases of acute or chronic dissection were treated. Twenty-six patients required replacement of the aortic valve, with annuloaortic ectasia being the most common indication (71%). Ten patients underwent concomitant coronary artery bypass grafting. The operative mortality rate for ascending aortic aneurysm repairs was 4%, and that for dissections was 18%. Five of 8 patients requiring aortic arch replacement survived. Most patients were studied angiographically before discharge. No complications were related to anastomotic hemorrhage, pseudoaneurysm formation, graft migration, or thromboemboli. Individual cases of phrenic nerve palsy, acute tubular necrosis, and transient ischemic attack, all of which resolved completely, were identified. The actuarial 5-year survival rate is 64%. We conclude that modification of the sutureless intraluminal ring graft to suit the pathology encountered at operation allows the quickest repair with the least chance of anastomotic complication.

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Surgical management of diseases of the ascending aorta and aortic arch is associated with high morbidity and mortality [1–4]. In part, these complications result from technical difficulties with the use of conventional tube grafts, including suture line hemorrhage through friable tissue [1, 5]. In addition, prolonged insertion times increase the risk of myocardial injury and cerebral ischemic damage. To avoid anastomotic complications and minimize graft insertion time, we began using sutureless intraluminal ring grafts for descending aortic dissections in 1976 and extended this practice to the ascending aorta in 1978. In this report, we review our 10-year experience with this device in the ascending aorta and aortic arch.

Material and Methods

Between 1978 and 1989, 49 patients underwent replacement of the ascending aorta or aortic arch with a sutureless intraluminal prosthesis. (The first eight devices were handmade in the Temple University machine shop. All remaining grafts were made by Bard, Inc [Billerica, MA].) Twenty-three of the patients were operated on during the first half of the study period, and 26 were operated on during the second half. Figure 1 summarizes patient profiles and treatment. Thirty men and 19 women were involved in the study; their ages ranged from 15 to 77 years (mean age, 57 years). The follow-up period was 104 months (mean follow-up, 49 months). Eight operations involved placement of the graft in the aortic arch, and 41 involved insertion into the ascending aorta. Fifteen patients (31%) were taken to the operating room under emergency conditions. Among the patients requiring replacement of a diseased portion of the ascending aorta, 13 had acute dissections, 4 had chronic dissections, and 24 had atherosclerotic aneurysms. Among the 8 patients requiring operation on the aortic arch, 4 had atherosclerotic aneurysms and 4 had dissections, two of which were acute. Twenty-six patients (53%) underwent aortic valve replacement at the time of their aortic operation; 20 of these individuals had aneurysmal disease. Eight patients (16%) required concomitant coronary artery bypass grafting. Four patients had an aortoatrial polytetrafluoroethylene (PTFE) shunt placed at the completion of the procedure. Most patients underwent digital subtraction angiographic evaluation of the ring graft before discharge from the hospital. A few patients underwent long-term follow-up with digital subtraction angiography, computed tomography, or magnetic resonance imaging to evaluate ring graft function. Serum hemoglobin and haptoglobin levels were measured in select patients to evaluate hemolysis.

Operative Technique

The sutureless intraluminal ring graft may be modified to suit the pathological condition found during replacement of the ascending aorta and aortic arch.

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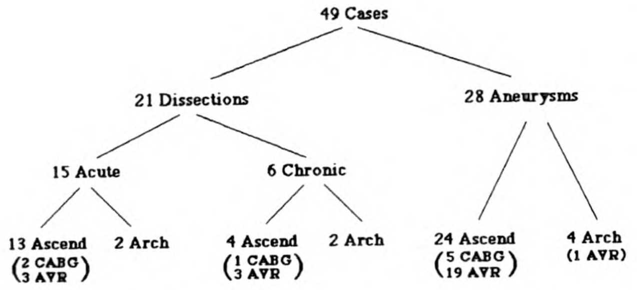

Fig 1. Flow chart of patients undergoing replacement of the ascending aorta and aortic arch shows underlying disease and treatment required. (AVR = *aortic valve replacement;* CABG = *coronary artery bypass grafting.)*

ACUTE DISSECTION. If the aortic valve is not involved or can be resuspended, the proximal spool of the prosthesis is fixed with five horizontal mattress sutures of 3-0 polypropylene placed at each aortic valve commissure and above each coronary ostium (Fig 2). The spool is secured in place with a 2-mm Dacron tie (Bard, Inc, Billerica, MA). The distal spool then is inserted and secured in place with another Dacron tie placed around the aorta.

ANEURYSM WITH AORTIC INSUFFICIENCY. In patients who require simultaneous aortic valve replacement, we remove the proximal ring and suture the Dacron graft to the valve using a running 3-0 polypropylene suture (Fig 3). We most commonly used a Björk-Shiley valve early in our experience, but later changed to the St. Jude prosthesis. After the composite graft is constructed, the device is inserted into the aorta in a fashion similar to the Bentall procedure [6]. Orifices are created in the graft and are secured at the coronary ostia with running 4-0 polypropylene sutures. The distal ring of the intraluminal device then is inserted, and the spool is secured permanently with external ligatures of nylon tape. Alternatively, we have inserted a valve with an attached PTFE graft and then secured the proximal ring of the intraluminal device within the PTFE sheath using Dacron tape ties. This method allows easier reconstruction of the coronary ostia. Even if the proximal ring is removed to construct an individualized proximal anastomosis, we believe that time is saved by retaining the distal spool for easy insertion. The aortic wall is closed about the graft at the completion of the procedure. If an aortoatrial fistula is deemed necessary, a PTFE graft 6 or 8 mm long is constructed; this graft often closes by the time of follow-up digital subtraction angiographic evaluation, and we have had no complications with these shunts.

ARCH ANEURYSM. Rapid replacement of diseased tissue is accomplished using the ring grafts (Fig 4). The grafts are elongated as needed either by suturing two ring grafts together or by using a PTFE graft as a sleeve into which

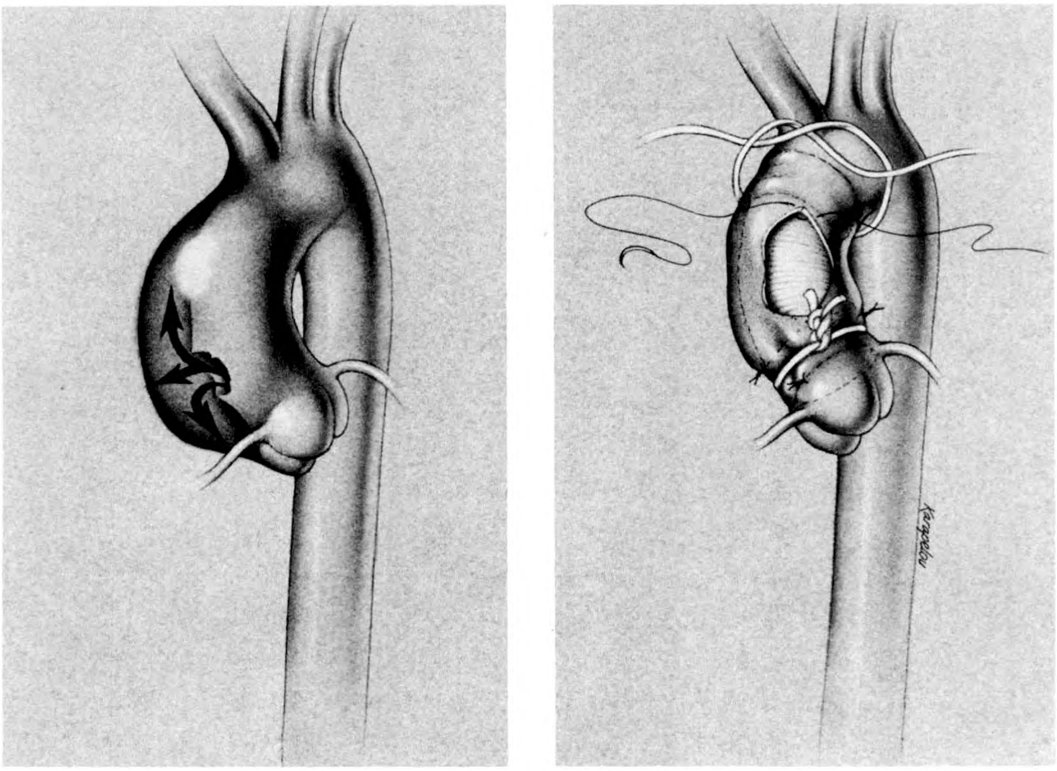
A
B

Fig 2. (A) Pathology encountered in an acute aortic dissection. The aortic valve is competent. (B) Repair is accomplished with a sutureless device secured above the aortic valve with several nylon sutures above the commissures, followed by Dacron tape ties around the spools and aortic wall.

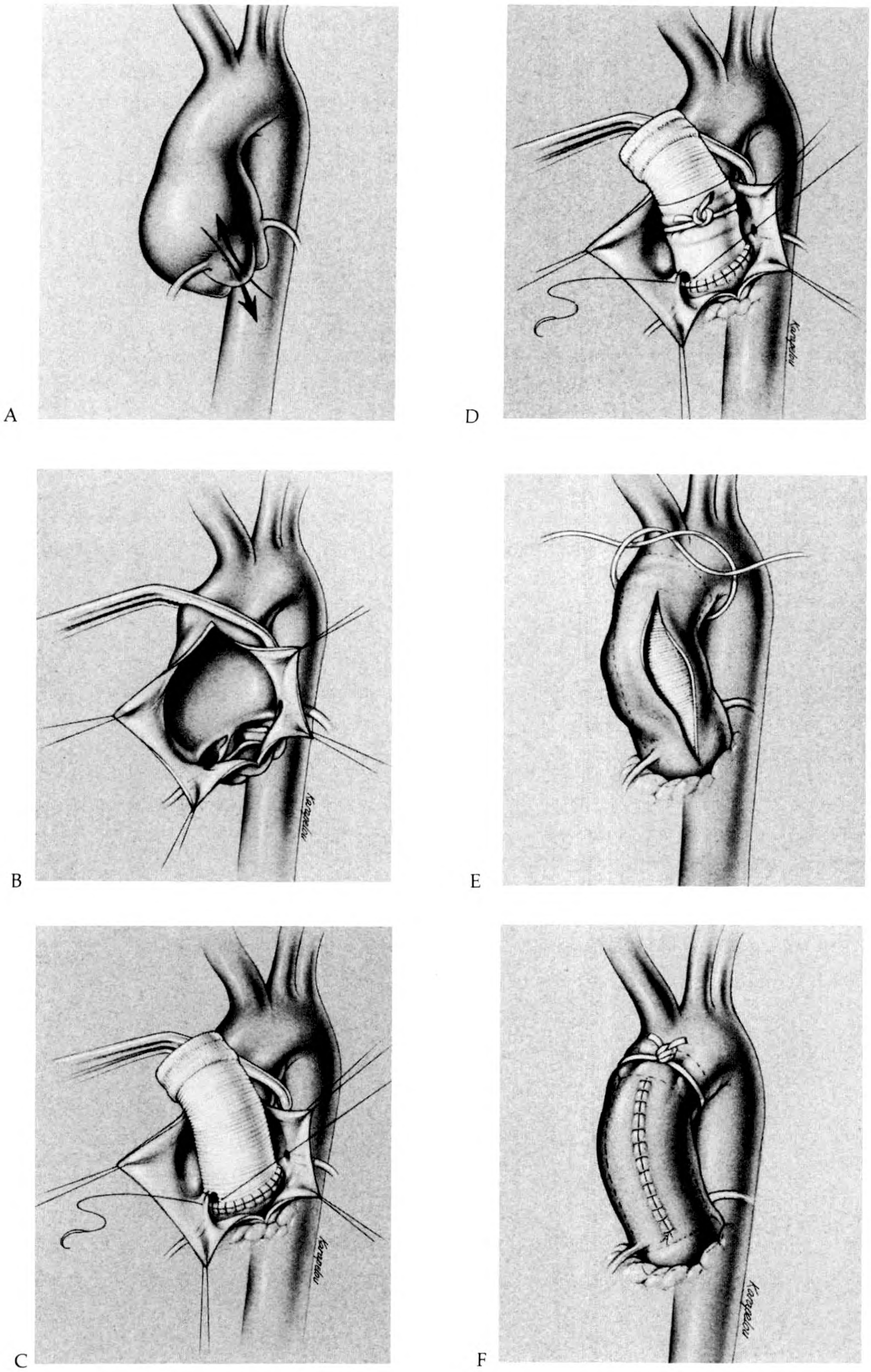

Fig 3. (A) An aortic aneurysm with aortic insufficiency. (B) The anterior aortic wall is incised to show the aortic valve annulus. (C) The proximal spool of a sutureless graft has been removed, and the free cuff is attached to an aortic prosthetic valve and sutured in place in the usual fashion, including reanastomosis of the coronary arteries. (D) Alternatively, a prosthetic valve attached to polytetrafluoroethylene material is inserted, and the proximal spool of a sutureless device is secured within the free end of the polytetrafluoroethylene graft with a Dacron tie. (E) No matter how the proximal anastomosis is accomplished, the distal spool is inserted and secured with Dacron tape. (F) The aortic wall is closed over the ascending aortic graft.

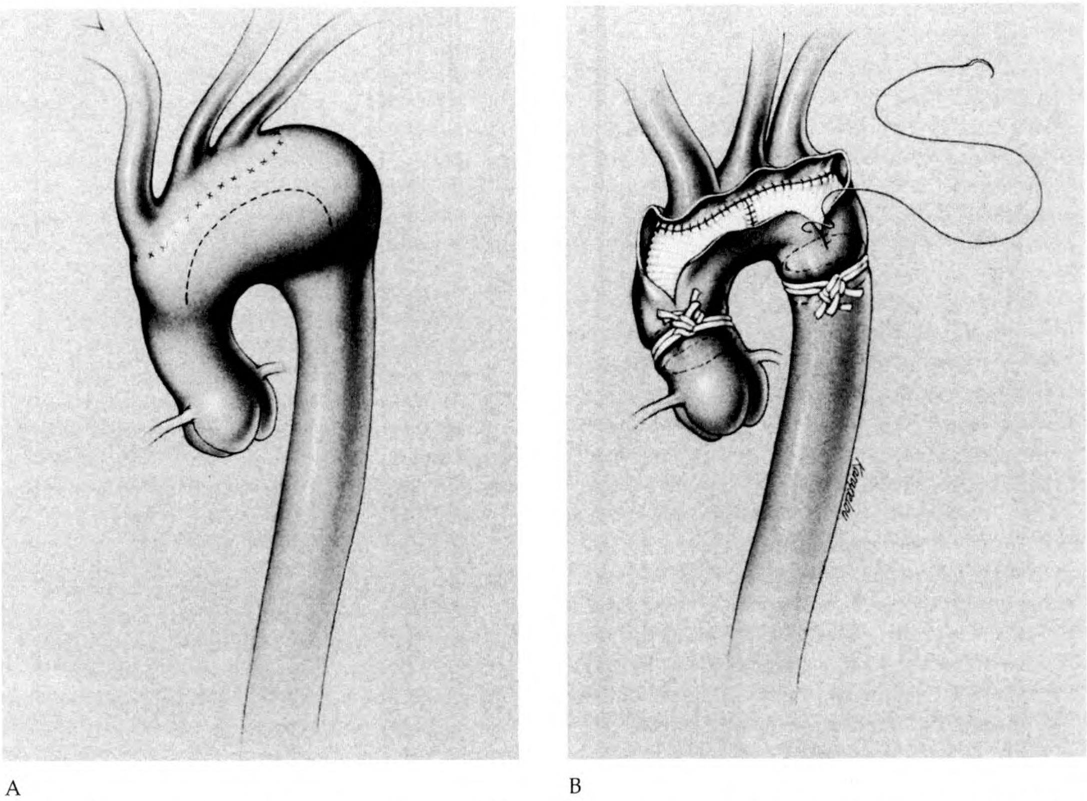

Fig 4. (A) An aortic arch aneurysm. (B) Two sutureless devices are joined together by removing adjoining rings and suturing the free ends together, thus leaving intact rings on either side. An island of tissue incorporating the arch vessels is anastomosed to the elongated graft. Time is saved by rapidly fixing the proximal and distal spools within the ascending and descending aorta.

the rings of each sutureless graft can be inserted. The latter technique allows the surgeon to elongate the intraluminal prosthesis as needed. In either case, an island of aortic tissue giving rise to the major vessels is anastomosed to the graft material, and the proximal and distal rings are secured using a single umbilical tape on each end. If the proximal graft must be tailored to incorporate the aortic wall tear or to include an aortic valve, the proximal ring is removed, and the distal ring alone is used.

Results

Intraoperative complications were uniformly related to hemodynamic compromise before operation. The mean aortic cross-clamp time was 35 minutes in uncomplicated sutureless ring graft placements. Procedures involving insertion of composite aortic valve-ring graft prostheses often required less than one hour of aortic clamping, although some combined procedures took longer.

There were four surgical deaths (10%) among patients undergoing replacement of the ascending aorta, all of which occurred within the first 24 hours after operation. Three of these deaths involved hemodynamically unstable patients who had emergency operations and intraoperative cardiac arrest. The other death occurred when ventricular failure developed in a patient with a chronic ascending aortic aneurysm who underwent concomitant aortic valve replacement. Three early deaths (37%) occurred in hemodynamically unstable patients undergoing emergency aortic arch replacement. One operative death (4%) was identified among the 24 patients (62%) requiring replacement of an ascending aortic aneurysm. Seventeen patients underwent operation to repair an acute or chronic ascending aortic dissection; three operative deaths occurred (18%). None of the deaths resulted from graft dysfunction.

Nonfatal early complications included individual cases of transient ischemic attack, wound infection, phrenic nerve palsy, acute tubular necrosis, and chest wall bleeding, which necessitated reoperation. All of these difficulties resolved without sequelae or morbidity. There was no evidence of graft dislodgement, graft infection, aortic bleeding, or pseudoaneurysm formation in the postoperative period. One patient with Marfan's syndrome required reoperation 18 days postoperatively to repair an acute dissection in the descending aorta that had not been present at the initial procedure.

At this time, 35 patients (73%) are still alive, with an actuarial 5-year survival rate of 64%. The leading causes of late death were arrhythmias and myocardial infarction. Randomly selected patients were followed with digital subtraction angiography, computed tomography, or magnetic resonance imaging and showed no evidence of graft migration, erosion, or thrombosis. In several patients, serum hemoglobin levels were checked at various intervals up to 4 years after insertion of a sutureless device. No hemolysis was evident from these studies. At autopsy, the aortic tissue adjacent to the spools was densely fibrotic and sometimes was completely replaced with fibrous tissue. No pseudoaneurysms have been identified. The grafts have remained intact without evidence of kinking or dislodgement.

Comment

Since Abbé [7] first used a thin vitrilline hourglass-shaped tube to repair severed femoral vessels in 1894, vascular surgeons have been interested in using a sutureless prosthesis to repair diseases of the aorta surgically. Because of the risks of prolonged ischemia during replacement of the aorta and because sutured anastomoses can be difficult when the aorta is soft and friable, a sutureless method was appealing. By 1912, Carrel [8] had attempted "intubation" of the aorta with metallic tubes. However, it was not until a decade ago that our group [9, 10] and others [11, 12] reported success using variations of intraluminal devices.

Our results using sutureless intraluminal devices in the ascending aorta are comparable with those reported with use of conventional sutured anastomoses. The mortality rate for ascending aortic aneurysms is reported to be 5% to 13% [1, 13], and that for ascending aortic dissections is 8% to 27%, depending on the acuteness of the aortic wall tear [14].

Bleeding complications, which have necessitated reoperation in 11% of patients in past studies [1], did not cause serious problems for our patients. Pseudoaneurysm formation, another potentially devastating complication, also was not identified in this study. Avoiding anastomoses with friable, diseased aortic tissue provided for these results. In addition, the operations were completed quickly owing to the ease with which the ring grafts can be inserted. Even if the encountered pathology required a proximal sutured anastomosis, time was saved by using a spool instead of sutured distal anastomosis. Partly as a result of these advantages, postoperative complications were reduced, and none of the patients who survived the initial 24-hour postoperative period died in the hospital.

Three possible complications may occur with insertion of a sutureless intraluminal prosthesis: (1) thrombosis or embolism, (2) hemorrhage or pseudoaneurysm development due to erosion of the wall of the aorta, and (3) migration of the prosthesis due to insufficient fixation. None of these complications has occurred in the 104-month follow-up of the patients in this study. Several technical developments provide for these results. We use a woven Dacron graft on surfaces exposed to blood to induce an adherent neointima and minimize the possibility of a thromboembolism. The graft also is preclotted by autoclaving in the patient's plasma for three minutes. The outer surface of the spools is lined with Dacron cloth, which induces sufficient scarring to hold the prosthesis in place [15]. Finally, the broad design of the spool and the vascular nature of the aortic wall make erosion after tying of the spool unlikely. This complication has never occurred in our patients.

Surgeons without experience with the sutureless intraluminal devices often use too wide or too long a graft for the involved aorta. Reduction of the aortic lumen by up to 70% produces no increase in intravascular hemolysis and creates no flow-related insufficiencies. For this reason, when selecting graft diameter, error on the side of a smaller graft is warranted. We size the ascending aortic lumen with valve obturators and choose a graft diameter that fits comfortably within the proposed vessel. In our experience, a 24-mm diameter graft is used most often; infrequently, we use devices 22 and 26 mm in diameter.

Use of too long a graft results in kinking, with serious hemodynamic complications. The Dacron grafts stretch 30% after intraaortic insertion; therefore, a graft length that is shorter than the diseased aortic segment should be selected. Again, too little graft is better than too much. If a composite PTFE device is used, the PTFE can be fixed to the ring after insertion, when a more precise determination of the optimal graft length has been made.

Incorrect placement of fixation ligatures on the spools is a final danger encountered during the learning process. We routinely place two ties on the spools and sometimes apply a third tie on the graft material itself between the spools to prevent blood leakage through the graft–spool interface. When stabilizing the spool, care must be taken to ensure that the posterior surface of the spool is in contact with the tie before tension is applied on the ligature. This avoids dislodgement of the device and prevents inadvertent injury to the aortic wall by the shearing force of the ligature pulling the aortic back wall over the spool.

Although sutureless intraluminal devices are especially useful in aortic dissections, we now are using these grafts routinely in aortic aneurysms and infected aortitis [16]. The advantages over sutured anastomoses are not as great; however, the reduction in operative time warrants use of a sutureless graft in these situations, especially if the patient's condition is unstable.

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Improved Myocardial Preservation During Cold Storage Using Substrate Enhancement

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This study was undertaken to determine whether substrate enhancement with L-glutamate during periods of cold storage would improve ventricular function in transplanted hearts. Thirty-one rabbit hearts were rapidly excised and perfused with Krebs-Henseleit buffer (37°C) on a Langendorff apparatus. They were arrested with hypothermic (4°C), crystalloid, potassium (25 mEq/L) cardioplegia and stored at 3°C for three hours, followed by reperfusion with Krebs-Henseleit buffer for one hour. Hearts were treated in one of several ways: Group 1 (n = 8) did not receive any L-glutamate and served as controls; group 2 (n = 8) had L-glutamate (4 mmol/L) added to both the cardioplegic and reperfusate solutions; group 3 (n = 5) received L-glutamate only before ischemia; group 4 (n = 5) received L-glutamate only in the cardioplegic solution; and group 5 (n = 5) received L-glutamate only in the reperfusate. Hearts receiving L-glutamate in the reperfusate with or without its addition to the cardioplegic solution (groups 2 and 5) had the best recovery of the first derivative of positive and negative change in left ventricular peak systolic pressure and no significant changes in left ventricular compliance. Pretreatment with L-glutamate alone (group 3) resulted in no better recovery than in group 1 hearts. We conclude that addition of L-glutamate to reperfusate solutions after periods of cold storage for transplantation enhances the recovery of ventricular function.

(Ann Thorac Surg 1990;50:80–5)

The paucity of available donor hearts and time restraints on storage and preservation have become major limiting factors in heart transplantation. It is therefore imperative that donor hearts have maximal myocardial protection during the periods of harvesting, cold storage, and subsequent reperfusion. Despite substantial improvements in methods of cold storage, current techniques may still result in depressed ventricular function [1]. Even in hearts with good hemodynamic function after three hours of cold storage, electron microscopic studies have showed cellular injury evidenced by significant mitochondrial and nuclear swelling on reperfusion [2].

Substrate enhancement with the amino acid L-glutamate minimizes ischemic damage when L-glutamate is added to both cardioplegia and reperfusate solutions after periods of ischemic arrest [3–6]. The protective effects of L-glutamate appear to arise from its ability to enter into transaminase reactions to form key Krebs cycle intermediates that are depleted during ischemia [7–10]. This study was therefore undertaken to determine whether substrate enhancement with L-glutamate during periods of cold storage would improve ventricular function in transplanted hearts. In addition, we sought to determine the specific time period (before ischemia, cold storage, or reperfusion) during which administration of L-glutamate would be most effective.

Material and Methods

Preparation

Thirty-one adult New Zealand rabbits (2 to 3 kg) were anesthetized with intravenous nembutal (50 mg/kg). Their hearts were rapidly excised, and the aortas were perfused with Krebs-Henseleit buffer supplemented with glucose (5 mmol/L) on a Langendorff apparatus gassed with 95% O_2 and 5% CO_2 with a pH of 7.4 at 37°C. The buffer was double-filtered through a 20-μm microfilter (Cobe Laboratories, Lakewood, CO) and a 1-μm glass microfilter (Whatman GF/A, Maidstone, England). All hearts were perfused at a mean aortic pressure of 75 mm Hg. Left ventricular temperature was monitored with a thermistor probe, and the temperature of the perfusate was measured with an NTM-100 digital thermometer (Wilton Webster Laboratory, Altadena, CA). The right and left ventricles were vented. The left atrium was incised, and a latex double-lumen balloon catheter was inserted into the left ventricle. One lumen was used for measuring left ventricular (LV) peak systolic pressure as well as its first derivative (dP/dt). The other lumen was used to infuse saline so that LV volume could be varied.

Measurements and Data Analysis

Variables of systolic function were measured using the intraventricular balloon after a 30-minute period of stabilization on the Langendorff apparatus. Aliquots of saline solution were injected into the LV balloon, and peak positive and negative dP/dt and peak systolic pressure were measured at varying balloon volumes. Developed pressure (DP) was calculated by subtracting left ventricu-

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Table 1. Recovery of Left Ventricular Performance, Compliance, and Coronary Flow[a]

	Group				
Variable	1	2	3	4	5
EDP (mm Hg; pre- vs postischemia)	31 ± 3 vs 45 ± 6[b]	29 ± 4 vs 33 ± 3	39 ± 7 vs 53 ± 6[b]	36 ± 11 vs 63 ± 7[b]	36 ± 10 vs 41 ± 1
DP (% recovery)	66 ± 3	72 ± 4	65 ± 4	77 ± 6	81 ± 2[c]
+dP/dt (% recovery)	66 ± 5	88 ± 5[c]	71 ± 8	80 ± 5	95 ± 5[c]
−dP/dt (% recovery)	79 ± 6	90 ± 10	62 ± 4	90 ± 6	95 ± 6
Coronary flow (mL/min)[d]					
Preischemia	63 ± 3	54 ± 5	56 ± 3	55 ± 5	59 ± 5
Postischemia	41 ± 3[b]	50 ± 4	45 ± 5[b]	41 ± 3[b]	51 ± 3

[a] Values are calculated at a balloon volume of 0.8 mL and expressed as mean ± standard error. [b] Significance: $p < 0.05$ versus preischemic values. [c] Significance: $p < 0.05$ versus group 1. [d] Mean aortic pressure = 75 mm Hg.

DP = developed pressure; dP/dt = first derivative of left ventricular pressure; EDP = end-diastolic pressure.

lar end-diastolic pressure (LVEDP) from peak systolic pressure. Developed pressure and peak positive and negative dP/dt were measured at increasing balloon volumes during preischemic and postischemic periods and then averaged for each experimental group. The data were expressed in both absolute numbers and as the percentage of recovery from preischemic values at a balloon volume of 0.8 mL.

Left ventricular compliance was assessed by measuring LVEDP at varying balloon volumes. A pressure–volume curve was constructed. Left ventricular end-diastolic pressure was recorded for both preischemic and postischemic periods and then averaged for each experimental group.

Coronary flow was measured from the right ventricular vent at a mean aortic pressure of 75 mm Hg over two successive one-minute periods. Flow measurements were made during the preischemic and postischemic periods with the heart in the beating empty state and then averaged for each experimental group.

All data are expressed as the mean ± standard error of the mean. Statistical evaluation between preischemic and postischemic measurements within each group was performed with paired Student's t test. Differences among the various groups were assessed using tests of analysis of variance in consultation with the Department of Biostatistics at the Boston University School of Medicine. Differences were considered significant at the $p < 0.05$ level.

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Experimental Groups and Protocols

After control measurements were made of LVEDP, DP, +dP/dt, −dP/dt and coronary flow, all hearts were arrested with a single dose (5 mL/kg) of hypothermic (4°C), crystalloid, potassium (25 mEq/L) cardioplegia and rapidly placed in a water-jacketed organ bath immersed in iced saline solution and stored at 3°C for three hours. Just before they were rewarmed, a second dose of hypothermic cardioplegia was administered (5 mL/kg). All hearts were then reperfused with Krebs-Henseleit solution (37°C) for one hour on the Langendorff apparatus, at which time postischemic measurements were made.

Hearts were treated in one of several ways. Group 1 (n = 8) hearts did not receive any L-glutamate and served as controls. For group 2 (n = 8) hearts, L-glutamate (4 mmol/L) was added to both the cardioplegic solution and the Krebs-Henseleit reperfusate solution. Group 3 (n = 5) hearts were pretreated with L-glutamate (4 mmol/L) by adding the amino acid to the Krebs-Henseleit solution and perfusing the hearts for 30 minutes before cold storage. They received no L-glutamate in either the cardioplegic or reperfusate solutions. Group 4 (n = 5) hearts received L-glutamate (4 mmol/L) only in the cardioplegic solution. Group 5 (n = 5) hearts received L-glutamate (4 mmol/L) only in the reperfusate.

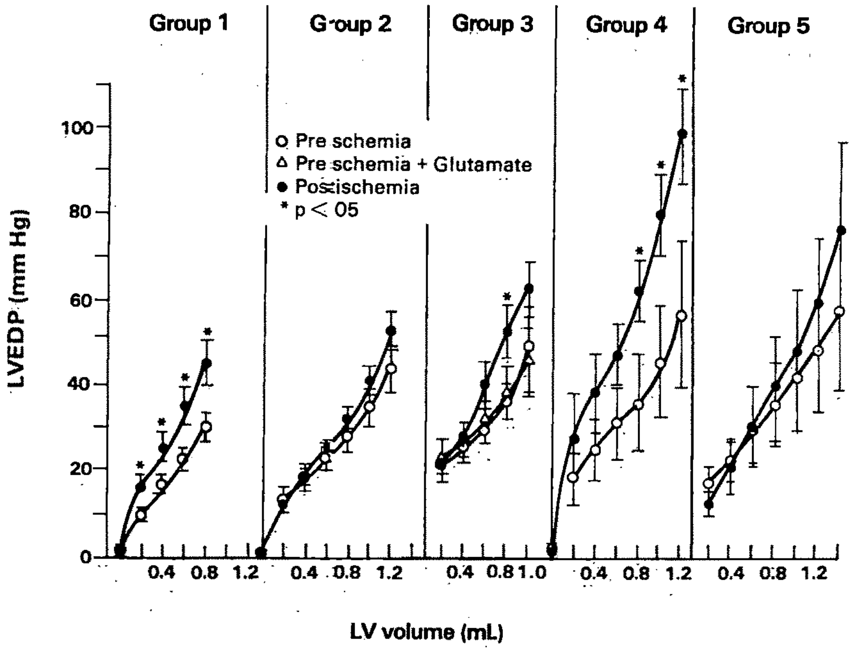
Results

Results are summarized in Table 1 and Figures 1 through 4.

Effects of Cold Storage in Hearts Without L-Glutamate (Group 1)

Hearts that did not receive L-glutamate in either the cardioplegic or reperfusate solutions showed significant depression in postischemic DP (103 ± 7 versus 67 ± 4 mm Hg at LV volume = 0.8 mL; $p < 0.02$; Fig 2), +dP/dt (17 ± 1 versus 11 ± 1 × 10^2 mm Hg at LV volume = 0.8 mL; $p < 0.05$; Fig 3) and −dP/dt (10 ± 1 versus 7 ± 1 × 10^2 mm Hg at LV volume = 0.8 mL; $p < 0.05$; Fig 4). Pressure–volume curves in the postischemic hearts showed a higher LVEDP at any given LV volume (31 ± 3 versus 45 ± 6 mm Hg at LV volume = 0.8 mL; $p < 0.05$; Table 1; Fig 1) demonstrating a decrease in LV compliance. Coronary flow was also significantly decreased in postischemic hearts (63 ± 3 versus 41 ± 3 mL/min; $p < 0.05$; Table 1).

Fig 1. Left ventricular compliance. (A) Hearts that did not receive L-glutamate in the reperfusate solution (groups 1, 3, and 4) showed significant changes in their postischemic pressure–volume curves. (B) Pretreatment with L-glutamate (group 3) failed to prevent changes in the postischemic pressure–volume relationship. (LV = left ventricular; LVEDP = left ventricular end-diastolic pressure.)



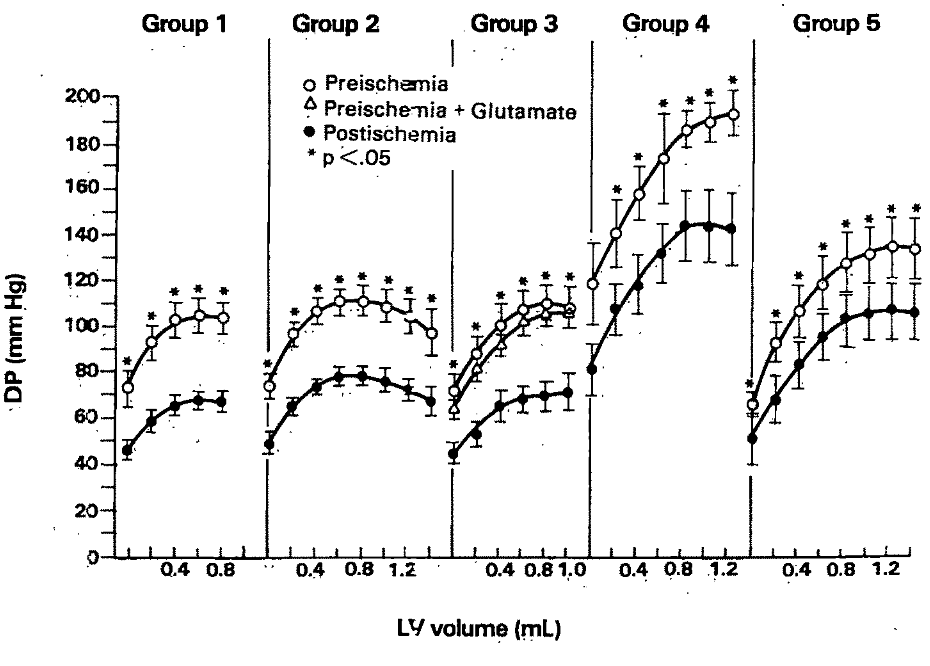
Effects of Adding L-Glutamate to Both Cardioplegic and Reperfusate Solutions (Group 2)

Hearts that received L-glutamate in both the cardioplegic and reperfusate solutions showed significantly better recovery of +dP/dt than group 1 hearts (88 ± 5 versus 66 ± 5; $p < 0.05$; Table 1; Fig 3). Although recovery of −dP/dt was greater than that of group 1 hearts (90% ± 10% versus 79% ± 6%; Table 1; Fig 4), it did not reach statistical significance with analysis of variance. Recovery of DP was unchanged from group 1 hearts (72% ± 4% versus 66% ± 3%; not significant [NS]; Table 1; Fig 2). No changes were observed in the postischemic pressure–volume curves, however, demonstrating complete recovery of LV compliance (29 ± 4 versus 33 ± 3 mm Hg at LV volume = 0.8 mL; NS; Table 1; Fig 1). Coronary flow remained unchanged during postischemic measurements (54 ± 5 versus 50 ± 4 mL/min; NS; Table 1).

Effects of Pretreatment with L-Glutamate (Group 3)

During the preischemic period, hearts perfused with L-glutamate–enriched Krebs solution showed no change in DP, +dP/dt, −dP/dt, and LVEDP–LV volume curves (Figs 1–4). As compared with group 1 hearts, pretreatment with L-glutamate did not improve recovery of postischemic DP (65% ± 4% versus 66% ± 3%; NS; Table 1; Fig 2), +dP/dt (71% ± 8% versus 66% ± 5%; NS; Table 1; Fig

Fig 2. Developed pressure. (A) Hearts receiving L-glutamate only in the reperfusate (group 5) had the best recovery of developed pressure. (LV = left ventricular; DP = developed pressure.)



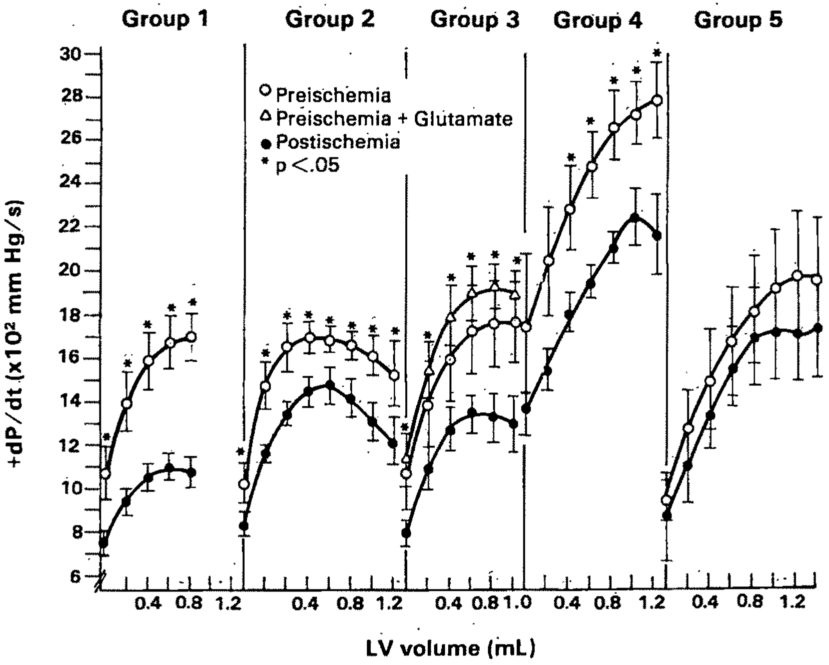


Fig 3: +dP/dt: (A) The absence of L*-glutamate in the reperfusate (groups 1, 3, 4) resulted in less recovery of postischemic contractility* (+dP/dt). (LV = *left ventricular.)*

3) or −dP/dt (62% ± 4% versus 79% ± 6%; NS; Table 1; Fig 4). Postischemic LVEDP–LV volume curves were significantly shifted to the left (LVEDP = 39 ± 7 versus 53 ± 6 mm Hg at LV volume = 0.8 mL; $p < 0.05$; Table 1; Fig 1), demonstrating a decrease in LV compliance. Coronary flow was significantly decreased (56 ± 3 versus 45 ± 5 mL/min; $p < 0.05$; Table 1).

Effects of Adding L*-Glutamate to the Cardioplegic Solution Only (Group 4)*

Hearts receiving L-glutamate only in the cardioplegic solution showed less protection from ischemic damage than hearts receiving L-glutamate in the reperfusate but recovered better than group 1 and group 3 hearts. Although DP (77% ± 6% recovery), +dP/dt (80% ± 5% recovery), and −dP/dt (90% ± 6% recovery) showed better recovery than in group 1 hearts, this did not reach statistical significance by analysis of variance (Table 1; Figs 2–4). The absence of L-glutamate in the reperfusate failed to protect these hearts from alterations in LV compliance (LVEDP, 36 ± 11 versus 63 ± 7 mm Hg at LV volume = 0.8 mL; $p < 0.05$; Table 1; Fig 1) and significant reductions in coronary flow (55 ± 5 versus 41 ± 3 mL/min; $p < 0.05$; Table 1).

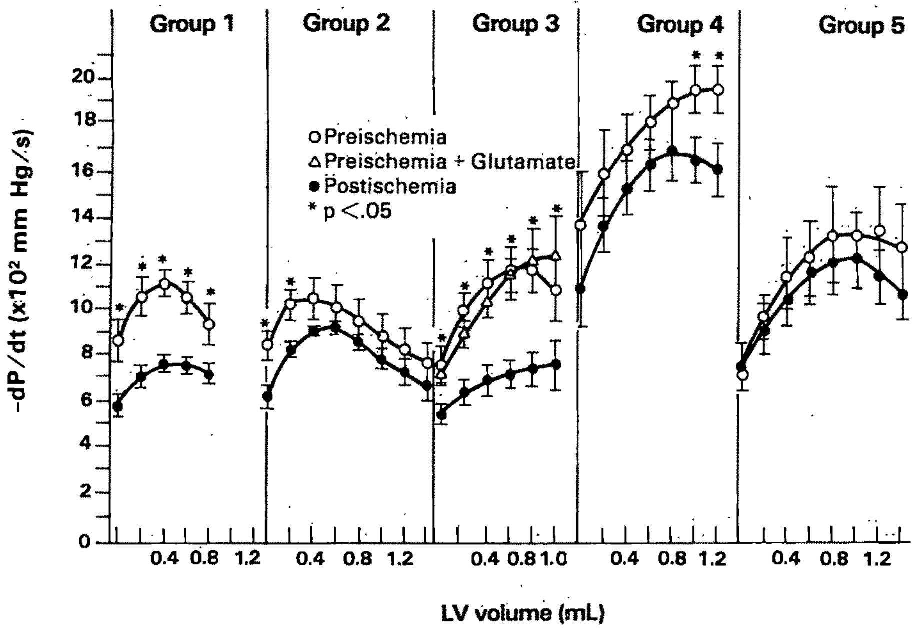


Fig 4. −dP/dt: (A) Absence of L*-glutamate in either the cardioplegic or reperfusate solutions (groups 1 and 3) resulted in less recovery of relaxation* (−dP/dt). (LV = *left ventricular.)*

Effects of Adding L-Glutamate to Only the Reperfusate Solution (Group 5)

Addition of L-glutamate to only the reperfusate solution resulted in superior recovery of all variables of LV function. Recovery of DP (81% ± 2%), +dP/dt (95% ± 5%), and −dP/dt (95% ± 6%) was more complete than that of groups 1 through 4 (Table 1; Figs 2 through 4). Postischemic LVEDP–LV volume curves returned toward preischemic levels (LVEDP, 36 ± 10 versus 41 ± 12 mm Hg at LV volume = 0.8 mL; NS; Table 1; Fig 1), and there was no significant change in coronary flow (59 ± 5 versus 51 ± 3 mL/min; NS; Table 1).

Comment

The superior recovery of myocardial function in L-glutamate–treated hearts after periods of cold storage is consistent with results of previous studies that demonstrated the beneficial effects of this amino acid after periods of ischemic arrest [3, 4, 6, 11, 12]. Dog hearts receiving a blood reperfusate including L-glutamate after 15 minutes of normothermic ischemic arrest had higher oxygen uptakes, more complete recovery of adenosine triphosphate, greater recovery of +dP/dt and −dP/dt, and the best recovery of compliance and stroke work index [3]. In both experimental and clinical studies, L-glutamate–enriched cardioplegic solutions resulted in superior recovery of adenosine triphosphate, stroke work index, and compliance [4, 6].

L-Glutamate is the only amino acid extracted by the normal myocardium. Together with L-aspartate, it has been shown to decrease significantly during periods of ischemia and anoxia [5, 13, 14]. Further evidence of L-glutamate's importance during ischemia was observed in clinical studies showing that hearts of patients with coronary artery disease extracted more L-glutamate than did hearts of individuals with normal coronary arteries [15]. During periods of ischemia, key Krebs cycle intermediates such as succinic acid may be depleted from the myocardium, leading to derangements in mitochondrial metabolism and adenosine triphosphate production [7]. Previous studies have shown that anoxia stimulates the metabolic conversion of L-glutamate to succinate [14, 16]. This conversion is the result of deamination reactions that transform L-glutamate to L-ketoglutarate, which continues in the Krebs cycle to form succinate. Further support of the transamination hypothesis comes from studies showing that the protective effect of L-glutamate can be blocked by adding aminooxyacetic acid, an inhibitor of mitochondrial transaminases [7–10, 12].

The current method of myocardial protection used by most transplant centers is single cold cardioplegic arrest followed by cold storage in a canister filled with sterile saline solution at 3° to 4°C [17]. Group 1 data in our study show that this technique can still result in significant depression of LV contractility and compliance (Table 1; Figs 1–4). The most optimal protection of LV systolic and diastolic function was achieved when L-glutamate was a component of the reperfusate solution (groups 2 and 5). When L-glutamate was a component of only the cardioplegic solution, variables of contractility (+dP/dt) and relaxation (−dP/dt) were preserved, but compliance was altered and coronary flow was decreased. Our study also shows that pretreatment with L-glutamate failed to protect the transplanted heart against ischemic injury, which suggests that treatment with L-glutamate is most crucial during the reperfusion period when key Krebs cycle intermediates may have been depleted during ischemia.

Because of limitations in existing cold storage techniques, more complicated perfusion devices have been studied to transport donor hearts [18]. Because cold storage is a far simpler technique, any intervention that may improve and prolong its protection will enhance its clinical applicability. Our future studies will try to determine whether L-glutamate, alone or in combination with other agents, can prolong the safe limits for cold storage techniques used in cardiac transplantation.

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Prophylactic Digitalization for Thoracotomy: A Reassessment

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A prospective, controlled, randomized clinical study of 140 patients undergoing elective thoracic operations over a period of 1 year in a regional referral unit was performed in which one group received digoxin and the other did not. The incidence of cardiac arrhythmia was compared in each group. Overall mortality was 5.7%. There was no significant difference in incidence of cardiac arrhythmia in each group, and we conclude that the prophylactic use of digoxin in elective thoracic operations should be revised.

(Ann Thorac Surg 1990;50:86–8)

Cardiac arrhythmias were first noted to be associated with surgical procedures in 1920 when digitalis was suggested as a treatment of choice [1]. This was followed by later reports indicating a specific and significant association of cardiac arrhythmia with thoracic surgical procedures [2–4], particularly in older persons [5]. Digitalis was discovered and first used successfully by William Withering more than 200 years ago. Its use fell into disrepute but became reestablished in the treatment of heart failure associated with atrial fibrillation in 1911 [6]. Development of atrial fibrillation and flutter with heart failure postoperatively were the most common cardiac complications of thoracic operations, leading to the suggestion that digoxin was indicated prophylactically [7]. Reports [8–10] on the effectiveness of prophylactic digoxin to control atrial fibrillation and other supraventricular tachyarrhythmias have been contradictory. The etiology of this complication is still not clearly understood, although several factors are likely to be involved [9]. The role of digitalis itself has come under review with increased awareness of toxicity, poor correlation between serum levels and efficacy, the potential of the drug itself to induce arrhythmias, and the availability of safer alternatives [10, 11]. This led us to reevaluate the prophylactic role of digitalis in a select group of patients.

Material and Methods

This prospective, controlled, randomized clinical study comprised 140 consecutive patients who underwent elective thoracotomy. Preoperative assessment included pulmonary function tests, electrocardiography (ECG), and arterial blood gas sampling. Patients were allocated either to receive digitalis preoperatively or not. A standard regimen of 500 μg at 6:00 PM and 10:00 PM the night before operation, followed by 250 μg with premedication, was administered. Postoperatively, 250 μg was administered daily for 9 days. Serum digoxin levels were measured by radioimmunoassay 6 hours after the oral dose on days 1, 3, and 5 postoperatively using the standard Amerlex kit (Amersham Int. Chemical Ltd, Amersham, England) (reference range, 1 to 2 μg/L), and dosage was adjusted accordingly. For ethical reasons, this was not a blind trial. One of us participated in each procedure to record details and assess the patients.

Constant-screen monitoring by ECG was chosen in preference to computerized long-term ECG, as this allows analysis of other factors such as hypoxia and hypokalemia to be assessed at the onset of arrhythmia, whereas the latter does not. Monitoring was commenced at the time of anesthetic induction and continued for at least 4 days. After 4 days, serial 12-lead ECG was performed on alternate days. We analyzed the electrocardiograms, which were confirmed blindly by a cardiologist. Serum K^+ and arterial blood gas estimations were performed at the onset of arrhythmias, which were treated as considered appropriate with full knowledge of existing drug therapy. Of 22 patients with documented myocardial disease, 14 received digoxin preoperatively.

Limitations of this study include use of a standard dose of digoxin unrelated to individual body surface area. As 88.5% of patients who received digoxin were within a serum digoxin level regarded as nontoxic and as the incidence of arrhythmias possibly related to toxicity were not significantly different for each group, we believe this to be an acceptable method in view of previous reports on the poor correlation between serum levels and efficacy [11–14]. Of all arrhythmias occurring in the digoxin group, 7% would not have been expected to be prevented by or related to digoxin therapy. Statistical analysis was by χ^2 using Yates' correction when appropriate.

Results

One patient died as the result of arrhythmia 4 days postoperatively. She had an uncomplicated upper lobectomy for benign disease and had cardiac arrest in asystole. Overall mortality was 5.7%. Patients were placed in one of

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Table 1. Number of Patients in Each Group, Number of Patients Receiving Digoxin, and Incidence of Arrhythmia[a]

	Pneumonectomy		Lobectomy		Esophago-gastrectomy		Open/Close		Other	
Variable	D	ND	D	ND	D	ND	D	ND	D	ND
Average age	65	60	59	64	66	74	77	50	62	73
No. of patients	11	8	23	31	10	10	11	4	9	13
Arrhythmia										
Number	7	5	11	11	4	2	4	2	3	4
Percentage	63	62	48	35	40	20	36	50	33	31

[a] $p > 0.5$ using Yates' correction.

D = digoxin given; ND = no digoxin given.

six groups: pneumonectomy, lobectomy, esophagogastrectomy, thoracotomy alone, hiatal hernia, or other, which includes patients undergoing anterior thoracotomy and biopsy, drainage of empyema, mediastinoscopy, thoracotomy with pleurectomy, stapling of bullae, and Heller's myotomy.

Of patients who received digoxin, 4% had digoxin levels below and 11.5% above the therapeutic range of serum digoxin at operation. Table 1 shows the patients in each group, the numbers of patients who received digoxin, and the incidence of arrhythmia. Ten patients in the hiatus hernia group did not have arrhythmia and have not been included in Tables 1 through 3, but this suggests that thoracotomy alone does not induce arrhythmia. The overall incidence of arrhythmia and, in particular, arrhythmias that may have been expected to have been prevented or related to digoxin therapy is 37%, with 41% in the group that received digoxin and 34% in the group that did not. Table 2 shows the forms of arrhythmia. As expected, atrial fibrillation accounts for almost 50% and arrhythmias related to digoxin therapy account for another 30%. Ten patients in the group that received digoxin and 12 in the group that did not required active intervention to treat their arrhythmias ($p > 0.5$). Only 6 patients with atrial fibrillation (12.5%) required treatment as opposed to all patients with supraventricular tachycardia and bradyarrythmias. In 2 patients, onset of arrhythmia could be related to hypoxia; in none could it be related to serum K^+ levels. The time of onset of arrhythmias was arbitrarily divided into less than 24 hours or more than 24 hours postoperatively. Table 3 shows the incidence of arrhythmia in relation to these times for each group and suggests an earlier onset of arrhythmia in the pneumonectomy group as opposed to other groups (<0.02) in the first 24-hour postoperative period. Our figures clearly show that most arrhythmias will occur in the first 24-hour period and more than half will begin in the perioperative period.

Table 2. Incidence of Arrhythmia

Arrhythmia	D	ND	Percentage
Atrial fibrillation	15	10	48
Atrial flutter	3	5	15
Supraventricular tachycardia	2	1	6
Bradyarrhythmia	4	2	12
Bigemini	2	1	6
Multiple ventricular ectopics	2	4	12
Other	0	1	2

D = digoxin given; ND = no digoxin given.

The average age of patients in each surgical group was greater than 60 years, and we could demonstrate no significant difference in incidence of arrhythmia between the group that received digoxin and the group that did not for patients aged less than versus greater than 60 years ($p > 0.5$). In terms of pathological process, there was no difference between the two groups. Of the 6 patients in whom tumor was identified in the pericardium or pulmonary artery, digoxin failed to control an arrhythmia in the 3 pneumonectomy patients to whom it was administered, 2 of whom had intrapericardial resections. Several anesthetic drugs were used in induction and maintenance of anesthesia. We could define no difference in incidence or onset of arrhythmia no matter which regimen was used. Of 22 patients with documented myocardial disease, 7 had arrhythmia with no significant difference between the groups ($p > 0.5$).

Comment

Several etiological factors of cardiac arrhythmia as a complication of thoracic operations have been identified, but the role and interaction of each remains unclear; increase

Table 3. Onset of Arrhythmias

	<24 h		>24 h		
Operation	D (%)	ND (%)	D (%)	ND (%)	p Value[a]
Pneumonectomy	71	100	29	0	<0.02
Lobectomy	64	36	36	64	>0.5
Esophagogastrectomy	75	50	25	50	>0.5
Open/close	50	100	50	0	>0.5
Other	100	75	0	25	<0.5

[a] By χ^2 test.

D = digoxin given; ND = no digoxin given.

in vagal activity and hypoxia are regarded as the most important factors [15]. Digoxin has been used prophylactically in an attempt to prevent or control these arrhythmias, but on an empirical basis. Limitation of the drug's efficacy, particularly in older persons, has been suggested by several groups of investigators [11, 12, 16, 17], who emphasize the dangers of arrhythmogenicity [14], toxicity [10], and preexisting pulmonary disease [18, 19].

The present prospective, controlled, randomized clinical study showed no statistically significant difference in incidence of arrhythmia between patients who received digoxin prophylactically and those who did not, using a standardized regimen of digitalization and monitoring postoperatively. This result differs from those of most other studies that claim a decrease in arrhythmias [7–9] but whose interpretation is complicated by their retrospective nature and variable methods of detecting arrhythmia [3, 8], digitalizing regimens [7–9], and groups under study [3, 7–10]. We believe that the methods used in our study have allowed us to detect a higher incidence (37%) than previously noted and to identify the 24-hour postoperative period and particularly the perioperative period as the most likely time of onset, whereas other investigators have identified the second to fourth days [15]. By identifying this period of maximum risk, we can adjust our efforts to detect and control arrhythmia.

The higher incidence of arrhythmia in patients undergoing pneumonectomy [3, 7] has been confirmed in this study. Manipulation of vagal fibers at the hilum, hypoxia, and direct invasion by tumor are considered important. All anesthetic agents currently used are potentially arrhythmogenic. Digoxin has been shown to protect from the negative inotropic effects of halothane [20] and a study of propofol has shown no association with arrhythmia [21, 22], but the higher incidence of arrhythmia in the perioperative and 24-hour postoperative period when anesthetic agents are still present is significant in pneumonectomy patients and suggests that an interaction may be important. Our study has shown no significant difference in incidence or outcome of arrhythmia in persons aged more than 60 years, although this may be related to our particular study group. The age of the patients who died (69 years) was not significantly different from that of survivors (65 years; $p > 0.5$). Of patients who underwent esophageal operations, cardiac arrhythmias occurred only in those with malignancy.

We conclude that development of arrhythmia remains a serious problem. We have demonstrated no significant benefit of prophylactic digitalization in control of arrhythmia in patients undergoing elective thoracic operations and suggest that its use should be revised. We suggest that study of etiological factors should be undertaken in controlled clinical studies so that prophylactic roles may be identified for the available alternative agents.

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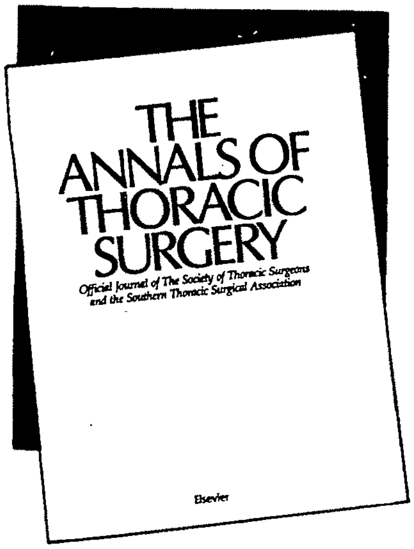
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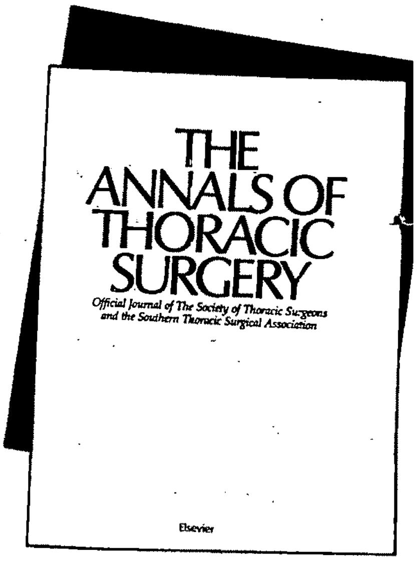

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Reversibility of Pulmonary Artery Hypertension in Aortic Stenosis After Aortic Valve Replacement

Gerald P. Tracy, MD, Michael S. Proctor, MA, MD, and Cathleen S. Hizny, BS

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Fifty-two surgical patients with isolated aortic valve stenosis were studied preoperatively and postoperatively to determine the incidence of pulmonary hypertension and its response to surgical intervention. Pulmonary artery systolic hypertension was classified as absent (group 1, <30 mm Hg), mild (group 2, 30 to 39 mm Hg), moderate (group 3, 40 to 59 mm Hg), and severe (group 4, >60 mm Hg). Thirty-seven of our patients (71%) had preoperative pulmonary hypertension. There was a positive correlation between left ventricular end-diastolic pressure and both systolic and diastolic pulmonary artery pressures preoperatively ($p < 0.001$). After operation we found a decrease in mean systolic pulmonary pressure in group 4, from 85.8 ± 23 mm Hg to 41.2 ± 10.4 mm Hg (a 52% decrease, $p < 0.001$), and in group 3, from 48.9 ± 5.9 mm Hg to 32.1 ± 7.1 mm Hg (a 34% decrease, $p < 0.001$). A significant decrease in the mean diastolic pressure was found only in group 4, in which the pressure decreased from 33.7 ± 8.7 mm Hg to 26.0 ± 7.6 mm Hg ($p < 0.05$). The operative mortality was 1.9%. Our data indicate that pulmonary artery hypertension in aortic stenosis is common, is related to end-diastolic pressure, and can be expected to improve in the early postoperative period.

(Ann Thorac Surg 1990;50:89–93)

The prognosis of patients with aortic stenosis and pulmonary hypertension without aortic valve replacement is poor [1, 2]. Studies of patients with pulmonary hypertension and isolated aortic stenosis who undergo aortic valve replacement have yielded conflicting results. Two studies have reported that preoperative pulmonary hypertension adversely affects prognosis [3, 4]. More recent reports challenge this conclusion [2, 5]. The differences may arise from the postoperative pulmonary vascular response to aortic valve replacement.

The effect of aortic valve replacement on pulmonary hypertension has not been well studied, though a single case has been reported [5]. We have, therefore, examined the preoperative and postoperative pulmonary artery pressures in a series of patients, with and without pulmonary hypertension, undergoing aortic valve replacement.

Material and Methods

Patient charts were retrospectively reviewed with approval of our Institutional Review Board. Fifty-two patients with isolated aortic stenosis were catheterized at our institution from January 1986 to June 1988. Other patients with aortic stenosis were excluded from the study because of multivalvar disease, the presence of aortic insufficiency of more than a trace amount, or serious coronary artery disease. The 52 patients with isolated aortic stenosis underwent aortic valve replacement and constitute the study group. None of the patients had clinical right heart failure.

Preoperative pulmonary artery pressures were obtained from cardiac catheterization reports. Also obtained, when available, were left ventricular pressures, aortic valve gradients, and aortic valve areas. When available, pulmonary vascular resistance was obtained in patients with mild or moderate hypertension. Aortic valve area was calculated according to the Gorlin formula [6]. Left ventriculograms, supravalvar aortograms, and coronary angiograms were also reviewed. Systolic function was evaluated by reviewing calculated ejection fractions and angiographers' descriptions of ventriculograms.

Postoperative pulmonary artery pressures were determined by averaging the last three recorded pressures in the surgical intensive care unit before removal of the Swan-Ganz catheter. These pressures were obtained at an average of 24 hours postoperatively. At the time of pulmonary artery pressure determinations the patients were not on cardioactive drugs, afterload reducers, intraaortic balloon pumps, or ventilators. Pulmonary vascular resistance data had not been obtained postoperatively.

Preoperative pulmonary artery systolic pressures were used to assign patients to one of four groups: group 1, normal (<30 mm Hg); group 2, mild (30 to 39 mm Hg); group 3, moderate (40 to 59 mm Hg); and group 4, severe (>60 mm Hg).

All patients underwent aortic valve replacement and no other cardiac procedures. The operations were performed on extracorporeal cardiopulmonary bypass with moderate systemic hypothermia and cold, potassium-containing cardioplegia.

A χ^2 test was used to determine if the groups differed with respect to sex. A one-way analysis of variance procedure was used to determine if there was a significant difference in age among the groups. Analysis of the

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Table 1. Clinical and Hemodynamic Profile of Patients by Group

Group	No. of Patients	Age (yr)	Male/ Female	Aortic Valve Gradient (mm Hg)	Aortic Valve Area (cm^2)	LVEDP (mm Hg)
1	15	65.1 ± 13.0	7/8	86.5 ± 17.5 (N = 12)[b]	0.40 ± 0.14 (N = 8)	12.3 ± 5.1 (N = 8)
2	10	60.8 ± 9.9	6/4	93.5 ± 28.2 (N = 10)	0.47 ± 0.43 (N = 8)	20.9 ± 8.2 (N = 10)
3	16	64.1 ± 7.8	11/5	78.3 ± 20.7 (N = 15)	0.46 ± 0.19 (N = 11)	22.6 ± 10.4 (N = 14)
4	11	65 ± 10.4	5/6	79.3 ± 25.7 (N = 11)	0.27 ± 0.09 (N = 8)	35.3 ± 11.5 (N = 11)
Total population	52	64.1 ± 10.3	29/23	83.7 ± 23.0	0.40 ± .24	23.2 ± 11.8

[a] Data are number of patients or mean ± standard deviation. [b] N is the number of patients for whom this data was available.

LVEDP = left ventricular end-diastolic pressure.

differences in diastolic and systolic pressures preoperatively and postoperatively for each group was performed by a matched-pair t-test. Correlation between variables was examined by testing the Pearson correlation coefficient. Probability values of less than 0.05 were considered significant.

Results

Thirty-seven of our 52 patients had pulmonary hypertension (71%). Twenty-seven patients had moderate or severe pulmonary hypertension (52%). Table 1 shows the distribution of patients among the groups, the number of male and female patients within each group, and the group averages for age, aortic valve gradient, aortic valve area, and left ventricular end-diastolic pressure. Tables 2 and 3 present the detailed information available on patients with moderate and severe pulmonary hypertension (groups 3 and 4).

The average age of the patients was 64.1 years. There were 29 men and 23 women. There was no statistically significant difference among the groups with respect to age or sex. Aortic valve gradients ranged from 33 to 140 mm Hg with an average of 83.7 ± 23.0 mm Hg. The average aortic valve area was 0.40 ± 0.24 cm^2. The average left ventricular end-diastolic pressure was 23.2 ± 11.8 mm Hg. There was a significant positive correlation between left ventricular end-diastolic pressure and pulmonary artery systolic pressure ($r = 0.58$; $p < 0.001$). There was also a significant positive correlation between left ventricular end-diastolic pressure and pulmonary artery diastolic pressure ($r = 0.625$, $p < 0.001$).

Table 2. Clinical and Hemodynamic Profile of Group 3: Aortic Stenosis and Moderate Pulmonary Hyertension

Patient No.	Age (yr)	Sex	Preop PA Pressures (mm Hg)	Preop PVR (dyne · s/cm^{-5})	Preop AoV Gradient (mm Hg)	Preop AoV Area (cm^2)	Preop LVEDP (mm Hg)	Postop PA Pressures (mm Hg)
1	67	F	46/18	670	33	0.5	5	30/10
2	46	M	40/15	333	90	. . .	20	19/8
3	72	M	55/20	718	71	0.4	24	30/22
4	60	M	45/15	408	. . .	. . .	22	25/14
5	69	M	49/14	337	80	0.4	21	36/10
6	79	M	45/18	519	80	0.5	25	36/21
7	65	F	47/. . .	. . .	101	0.3	19	34/21
8	58	M	56/18	502	106	. . .	14	35/22
9	66	M	56/26	. . .	80	. . .	. . .	31/12
10	64	F	45/12	292	96	0.3	33	30/11
11	69	F	42/18	. . .	48	. . .	26	40/22
12	59	M	46/11	408	90	0.5	32	29/11
13	58	M	57/19	400	74	0.5	46	24/18
14	64	M	44/18	366	55	0.6	6	48/22
15[a]	72	F	59/21	748	70	0.2	24	27/24
16	57	M	50/20	. . .	100	0.3	20	40/18

[a] This patient died postoperatively of sepsis.

AoV = aortic valve; LVEDP = left ventricular end-diastolic pressure; PA = pulmonary artery; PVR = pulmonary vascular resistance.

Table 3. Clinical and Hemodynamic Profile of Group 4: Aortic Stenosis and Severe Pulmonary Hypertension

Patient No.	Age (yr)	Sex	Preop PA Pressures (mm Hg)	PVR (dyne · s/cm^{-5})	AoV Gradient (mm Hg)	AoV Area (cm^2)	LVEDP (mm Hg)	Postop PA Pressures (mm Hg)
1	65	F	70/19	1,478	44	0.4	19	53/29
2	60	F	65/35	1,286	85	0.3	35	27/14
3	63	M	105/40	1,233	100	0.3	45	43/39
4	75	F	65/25	1,022	80	. . .	27	39/28
5	58	F	100/50	1,837	80	. . .	33	45/27
6	77	F	131/27	1,600	115	0.17	27	49/26
7	45	F	65/42	1,543	125	0.16	42	31/19
8	77	M	107/38	1,190	55	0.34	35	55/32
9	78	M	91/35	1,728	69	0.18	30	51/33
10	58	M	85/30	. . .	55	0.3	60	27/23
11	61	M	60/30	761	64	. . .	. . .	33/16

AoV = aortic valve; LVEDP = left ventricular end-diastolic pressure; PA = pulmonary artery; PVR = pulmonary vascular resistance.

The evidence on systolic function was examined in groups 3 and 4. In group 3 we were able to assign 13 of 16 patients to systolic functional categories: normal, 6; mildly depressed, 4; and moderately depressed, 3. In group 4, systolic function was evaluated in 9 of 11 patients: normal, 2; mildly depressed, 1; moderately depressed, 5; and markedly depressed, 1.

Preoperative and postoperative pulmonary artery pressures are compared in Table 4. Postoperatively there was a slight increase in the systolic pulmonary artery pressures (not significant) and in the diastolic pulmonary artery pressures ($p < 0.001$) in the normotensive patients (group 1). There were no significant changes in pulmonary artery pressures in the mildly hypertensive group (group 2). In group 3 the systolic pulmonary artery pressure fell from 48.9 ± 5.9 mm Hg preoperatively to 32.1 ± 7.1 mm Hg postoperatively ($p < 0.001$). In the same group the pulmonary artery diastolic pressure was reduced from 17.5 ± 3.8 mm Hg preoperatively to 16.3 ± 5.6 mm Hg postoperatively (not significant). In group 4 the systolic pulmonary artery pressure fell from 85.8 ± 23.0 mm Hg preoperatively to 41.2 ± 10.4 mm Hg postoperatively ($p < 0.001$). The diastolic pressure in this group declined from 33.7 ± 8.7 mm Hg preoperatively to 26.0 ± 7.6 mm Hg postoperatively ($p < 0.05$). Mean preoperative pulmonary vascular resistance in group 3 was 475 ± 158 dyne · s/cm^{-5} (Table 2); in group 4 it was 1368 ± 332 dyne · s/cm^{-5} (Table 3).

Table 4. Effect of Aortic Valve Replacement on Pulmonary Artery Pressures

Group	Pressure	Pulmonary Artery Pressure: Preoperative (mm Hg)	Pulmonary Artery Pressure: Postoperative (mm Hg)	p Value
1	Systolic	24.3 ± 3.9	27.1 ± 6.2	0.132
	Diastolic	7.5 ± 3.5	15.4 ± 4	<0.001
2	Systolic	33.7 ± 3.1	30.4 ± 7.5	0.128
	Diastolic	14.5 ± 6.2	17.5 ± 2.9	0.116
3	Systolic	48.9 ± 5.9	32.1 ± 7.1	<0.001
	Diastolic	17.5 ± 3.8	16.3 ± 5.6	0.605
4	Systolic	85.8 ± 23.0	41.2 ± 10.4	<0.001
	Diastolic	33.7 ± 8.7	26.0 ± 7.6	<0.05

Data are shown as mean ± standard deviation

There was only one postoperative death for an operative mortality of 1.9%. This patient (patient 15, Table 2) died of sepsis postoperatively.

Comment

Our evaluation of pulmonary hypertension in aortic stenosis was prompted by consideration of aortic valve replacement in a patient with aortic stenosis and a pulmonary systolic pressure of 131 mm Hg. The responses of several prominent cardiologists and cardiac surgeons, when asked about the expected fate of this pulmonary hypertension, were couched in such terms as "in my experience," "in my opinion," and "my bias is" pulmonary hypertension decreases after aortic valve replacement. We believed that the answer to such a potentially important question should not be left to mere opinion and conjecture, but should instead be examined in a series of patients and recorded in the literature.

The finding of pulmonary hypertension in isolated aortic stenosis was not common in earlier studies [7, 8]. Recently, however, Johnson and associates [2] reported a 50% prevalence of pulmonary hypertension in a population with aortic stenosis that had not undergone operation. Our prevalence of 71% is the highest thus far identified. The development of pulmonary hypertension in patients with aortic stenosis has been attributed to a deterioration in left ventricular diastolic function. Johnson and associates [2] found a significant correlation between left ventricular end-diastolic pressure and pulmonary artery systolic pressure. We have confirmed this correla-

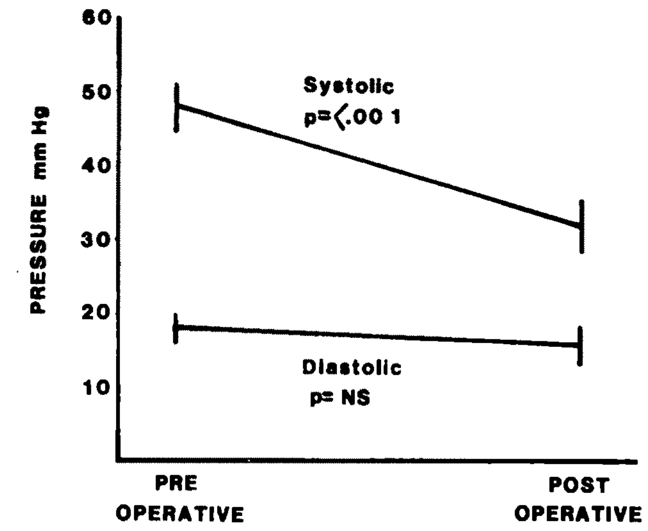

Fig 1. Changes in mean systolic and diastolic pulmonary artery pressure after aortic valve replacement in group 3. Vertical lines *represent ± one standard deviation.*

tion. We have also established a significant positive correlation between left ventricular end-diastolic pressure and pulmonary artery diastolic pressure in isolated aortic stenosis.

Our findings support the argument that deterioration in left ventricular diastolic function may be involved in the etiology of pulmonary hypertension in aortic stenosis.

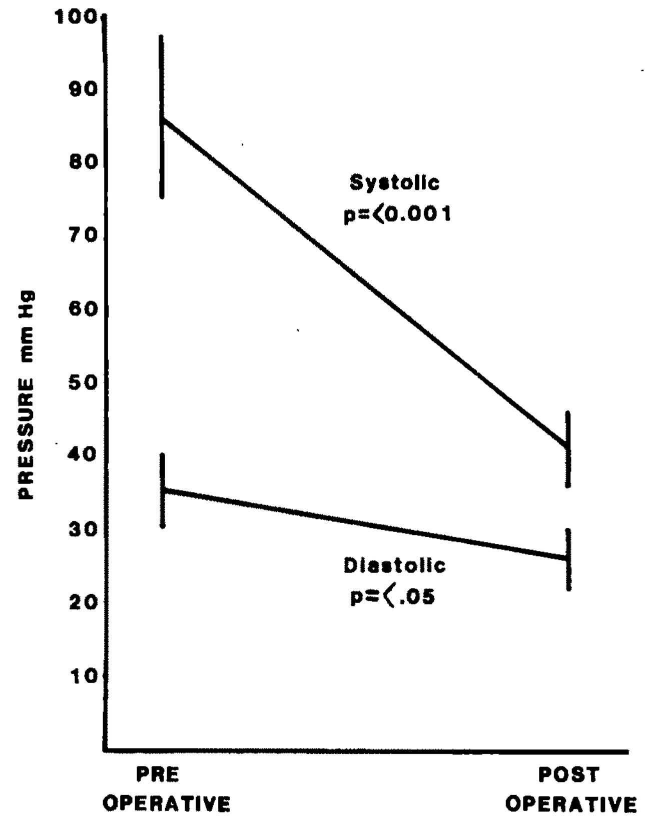

Fig 2. Changes in mean systolic and diastolic pulmonary artery pressure after aortic valve replacement in group 4. Vertical lines *represent ± one standard deviation.*

The mild postoperative increase in pulmonary artery pressures noted in the normotensive group may reflect a change in the patient's volume status. In light of this mild upward trend of pulmonary artery pressures in the normotensive patients (group 1), the dramatic fall in pulmonary pressures among the more severely hypertensive patients (groups 3 and 4) is all the more noteworthy. After aortic valve replacement there was a rapid and highly significant decrease in the pulmonary artery systolic pressures in groups 3 and 4. The systolic pulmonary pressures in group 3 fell by 34% (Fig 1), and those in group 4 fell by 52% (Fig 2). A significant but smaller decrease in pulmonary artery diastolic pressures was noted postoperatively in group 4.

The previously reported patient in whom pulmonary artery pressures were measured before and after aortic valve replacement also showed a decrease in pulmonary artery pressures postoperatively [5].

The rapid postoperative decrease in elevated pulmonary artery pressures after aortic valve replacement parallels the findings in successful mitral valve operations [9]. The rapidity of the improvement suggests that pulmonary artery hypertension in aortic stenosis is reactive and does not represent fixed pulmonary hypertension due to underlying pulmonary vascular disease. This improvement may reflect improved left ventricular end-diastolic pressure.

Questions remaining for future investigation include the effect of aortic valve replacement on pulmonary vascular resistance and left ventricular systolic function. Preoperative pulmonary vascular resistance was markedly elevated in our patients with moderate and severe pulmonary hypertension. Left ventricular function was also depressed in most of these patients. We do not have postoperative data for comparison in these two areas.

Our findings indicate that in patients with aortic stenosis there is a much higher incidence of pulmonary hypertension than previously reported. Our findings also support an optimistic prognosis for patients with aortic stenosis and even marked pulmonary hypertension who undergo aortic valve replacement. A rapid improvement in the systolic and diastolic pulmonary artery pressures after aortic valve replacement in patients with the most severe levels of pulmonary hypertension can be expected early in the postoperative period.

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Feasibility of Reversible Pulmonary Artery Banding: Early Results and Intermediate-Term Follow-up

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Development of a reversible pulmonary artery band might obviate the need for a second cardiac surgical procedure in children with some forms of congenital heart disease. We evaluated a segmented Silastic-coated Dacron mesh band 2 to 4 mm wide sewn together with absorbable 2-0 polydioxanone suture for use as a reversible pulmonary artery band. Nine puppies 6 to 8 weeks old (mean weight, 5.8 kg) underwent placement of this pulmonary artery band. All survived the operation with a mean initial systolic gradient of 6.5 ± 1.6 mm Hg and underwent cardiac catheterization at monthly intervals for 3 months. Two puppies died of right ventricular failure. The remaining puppies underwent balloon angioplasty with balloons 20 to 25 mm in diameter. No complications resulted from balloon angioplasty, but 1 puppy died 24 hours later of unidentified causes. Balloon angioplasty decreased the mean gradient from 46.7 ± 6.8 mm Hg to 6.7 ± 2.6 mm Hg. Angiography showed an increase in mean diameter of the site of the pulmonary artery band from 5.2 ± 1.0 to 10.8 ± 1.7 mm Hg. There was no evidence of vessel injury on angiograms. Fourteen months after balloon angioplasty, the mean gradient was 22.3 ± 17.0 mm Hg. Our data demonstrate that a functionally reversible pulmonary artery band constructed of segmented Silastic-coated Dacron mesh and 2-0 polydioxanone suture is feasible.

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Pulmonary artery banding was described by Muller and Damman in 1952 for palliative treatment of congenital cardiac defects with major left-to-right shunting [1, 2]. The procedure is used as a temporizing measure to preserve the option of later correction of a congenital abnormality or as definitive palliation [3, 4]. This has proved to be an effective modality of treatment; however, there may be substantial morbidity and mortality associated with pulmonary artery banding and debanding [4, 5]. In addition, ventricular septal defects, especially in the muscular ventricular septum, can close spontaneously after pulmonary artery banding [6]. Children in whom pulmonary artery bands are placed still must undergo another operation with cardiopulmonary bypass to remove the bands. The ability to place a band the effects of which could later be eliminated nonsurgically might decrease the morbidity and mortality associated with the subsequent surgical procedure. In some instances surgical intervention could be avoided altogether.

The development of balloon angioplasty to dilate stenotic valves [7–9] and arteries [10, 11] has made available a new technique to relieve obstruction such as that resulting from pulmonary artery banding. The feasibility of applying a band that can be dilated using the balloon angioplasty technique has been evaluated in animals [12–14]. Lindberg and colleagues [12] demonstrated successful balloon dilation of pulmonary artery bands made of Dacron tape secured with a 5-0 Prolene suture in dogs. These investigators described an immediate drop in systolic pressure gradient but were able to provide 6-month follow-up data on only a single dog.

In another investigation [13], two different banding materials were used on pulmonary or systemic arteries. Bands of cotton umbilical tape secured with 8-0 silk sutures were used in 11 dogs, and bands of a stainless steel fatigued helix encased in silicone rubber tubing were used in 4 dogs. Immediate relief of the systolic pressure gradient was achieved in each animal, but no follow-up was available. Using an absorbable suture (Vicryl; Ethicon), Rocchini and associates [14] demonstrated successful relief of obstruction with balloon angioplasty. A recent abstract by the same group [15] reported that relief of obstruction created by the pulmonary artery band persisted for at least 6 months after balloon angioplasty.

Although these studies are encouraging, one provides only short-term follow-up results and the other uses a technique not usually employed in the clinical setting. We therefore undertook this study to evaluate the technique of applying a reversible pulmonary artery band made of overlapping segments and to obtain longer follow-up evaluation.

Material and Methods

Nine puppies 6 to 8 weeks old with a mean weight of 5.8 kg (range, 4.1 to 7.3 kg) underwent pulmonary artery

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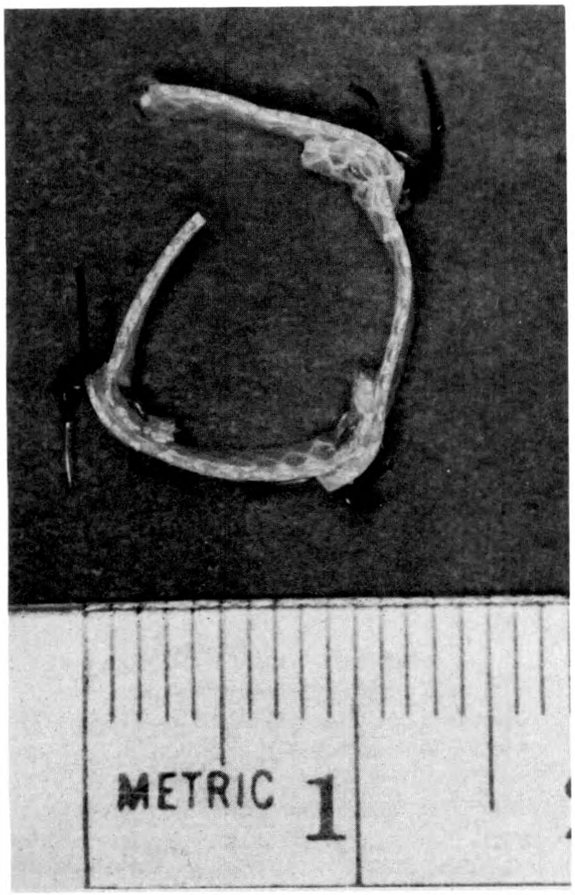

Fig 1. Segmented Silastic band. Segments were attached using polydioxanone suture.

banding. Each reversible band was constructed of Dacron mesh 2 to 4 mm wide coated with Silastic (Dow Corning, Midland, MI). Ten- to 12-mm lengths were sutured together with overlapping ends (Fig 1). A single 2-0 polydioxanone mattress suture was placed at the junction of the segments. In each instance, four connected segments provided enough length for a satisfactory pulmonary artery band.

Anesthesia was induced with thiamylal sodium and maintained with enflurane. All bands were placed through a left thoracotomy. Immediately after banding, measurements of right ventricular and pulmonary artery pressures were made by direct needle puncture. Postoperatively, all puppies underwent cardiac catheterization using percutaneous technique at 1-month intervals for 3 months.

Balloon angioplasty was accomplished 3 months later through the femoral vein with balloons 3 to 5 cm in length and 20 to 25 mm in diameter (Mansfield Scientific, Inc, Mansfield, MA). The balloon size was determined from the diameter of the nonstenotic main pulmonary artery as measured from an angiogram made before angioplasty. A balloon with a diameter approximately 20% greater than that of the pulmonary artery was chosen. After angioplasty, repeat pressure measurements were recorded across the band site. The animals were allowed to recover from anesthesia and were returned to their cages. Each puppy underwent repeat catheterization 1 month, 6 months, and 14 months after balloon angioplasty. None underwent repeat angioplasty. After the final catheterization, the animals were killed for gross anatomical examination of the right ventricle, pulmonary valve, and pulmonary artery band site.

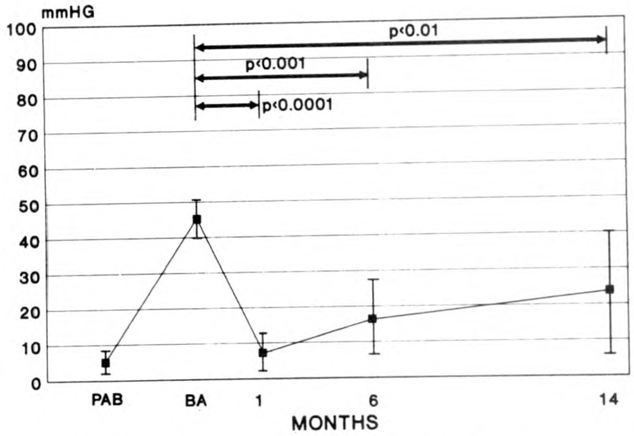

Fig 2. Systolic gradient (mean ± standard error of the mean) at time of pulmonary artery banding (PAB), time of balloon angioplasty (BA), and during 14 months of follow-up.

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 85–23, revised 1985.).

All data are presented as the mean ± the standard error of the mean. Means were compared using the paired *t* test, and multiple comparisons over time were analyzed using analysis of variance and Duncan's multiple range test [16]. A *p* value of 0.05 determined significance. All tests were two-sided.

Results

All puppies survived the operation and were found to have an immediate postoperative systolic gradient of 6.5 ± 1.6 mm Hg (Fig 2). One month later, the gradient had increased to 23.0 ± 6.6 mm Hg and the right ventricular systolic pressure had risen to 39.9 ± 10.6 mm Hg (Fig 3). The gradient and the right ventricular systolic pressure increased progressively until they reached 46.7 ± 6.8 (see Fig 2) and 64.7 ± 5.2 mm Hg (see Fig 3), respectively, by the third postoperative month.

Two animals died of right ventricular failure before balloon angioplasty. The remaining 7 puppies underwent successful angioplasty. No complications occurred with the dilation procedure, but 1 puppy died the day after successful angioplasty during which the pressure gradient was decreased from 88 mm Hg to 15 mm Hg. Postmortem examination revealed no major trauma to the right ventricle or pulmonary artery. The cause of death in this animal remains undetermined.

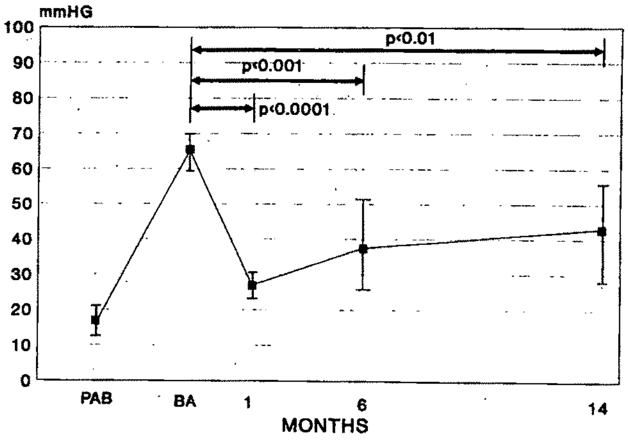

Fig 3. Right ventricular systolic pressure (mean ± standard error of the mean) throughout experimental period. Abbreviations are the same as in Figure 2.

Data from the remaining 6 animals are reported here. Balloon angioplasty decreased the mean systolic gradient from 46.7 ± 6.8 mm Hg to 6.7 ± 2.6 mm Hg and reduced the mean right ventricular systolic pressure from 64.7 ± 5.2 mm Hg to 29.2 ± 3.8 mm Hg (Table 1). One month later, the mean gradient was essentially unchanged at 7.5 ± 5.3 mm Hg, and the mean right ventricular systolic pressure was only 25.7 ± 2.7 mm Hg. At 14 months after balloon angioplasty, the mean gradient and right ventricular systolic pressure remained significantly ($p < 0.01$) lower, although there was a trend toward increasing values ($p = 0.01$) over time.

Cardiac output was not measured directly at the time of balloon angioplasty or during follow-up catheterizations. However, none of the animals exhibited signs of cardiac failure, and they all had normal systemic arterial pressure during each of the procedures.

By angiography, the mean diameter of the pulmonary artery band site was 5.2 ± 1.0 mm before balloon angioplasty. After that procedure, the mean diameter increased to 10.8 ± 1.7 mm. There was no angiographic evidence of injury to the pulmonary artery either during the procedure or at the 1-month catheterization after angioplasty.

At postmortem examination, the segmented band was found to be encased in a fibrous capsule. Each piece of the band was easily removed from the capsule, and there was no evidence of the polydioxanone suture used to connect the pieces and apply the band. A fibrous ridge was noted on the intimal surface of the main pulmonary artery at the band site, but there was no evidence of tears in the artery or damage to the right ventricular outflow tract.

Comment

Physiologically, pulmonary artery banding creates an increase in right ventricular outflow resistance, thereby decreasing left-to-right shunting and pulmonary blood flow. This relieves congestive heart failure in some forms of congenital heart disease and helps protect the patient from pulmonary vascular hypertension. The primary use of pulmonary artery banding has been in patients with congestive heart failure due to ventricular septal defects, as well as in patients with more complicated defects such as transposition of the great arteries with ventricular septal defect, double-outlet right ventricle, single ventricle, and truncus arteriosus [4]. The mortality associated with pulmonary artery banding is reported to be between 5% and 25% [4, 5]. Combined banding and debanding with corrective procedures can be associated with an overall mortality as high as 16% in patients with ventricular septal defects and up to 65% in patients with more complex anomalies [4].

Removal of a pulmonary artery band is performed under cardiopulmonary bypass, which in most instances is associated with repair of the primary cardiac defect. Debanding usually involves a longitudinal incision along the pulmonary artery trunk including the band site, and a patch is necessary to repair the stenotic pulmonary artery. The mortality and morbidity associated with application of a pulmonary artery band and subsequent debanding

Table 1. Results of Pressure Measurements in Growing Dogs With Pulmonary Artery Banding and Subsequent Balloon Angioplasty

	Weight (kg)			Right Ventricular Systolic Pressure (mm Hg)			RV–PA Gradient (mm Hg)		
Dog No.	At PAB	At BA	At Final Catherization	Before BA	Immediately After BA	Late After BA	Before BA	Immediately After BA	Later After BA
1	5.4	15.0	22.7	70	30	25	53	5	7
2	4.1	10.9	21.8	70	25	70	55	5	52
3	5.4	13.2	31.8	68	25	48	50	5	33
4	6.4	14.6	34.1	60	35	38	40	5	16
5	7.3	16.4	34.1	60	30	38	42	10	21
6	5.9	15.5	29.5	60	30	32	40	10	5
Mean	5.75 ± 1.1	14.3 ± 2.0	29.0 ± 5.5	64.7 ± 5.2	29.2 ± 3.8	41.8 ± 15.8	46.7 ± 6.8	6.7 ± 2.6	22.3 ± 17.0

[a] Data are shown ± the standard error of the mean.

BA = balloon angioplasty; PA = pulmonary artery; PAB = pulmonary artery banding; RV = right ventricle.

and the improving expertise in cardiac surgical procedures have resulted in an increasing trend toward early repair of congenital cardiac defects in infants. Nevertheless, a role for pulmonary artery banding remains.

Development of balloon angioplasty as a nonsurgical method to relieve obstruction makes the creation of a reversible band an attractive therapeutic modality. Numerous reports [7–11] have described success using balloon angioplasty and valvoplasty. The earliest and most extensive experience involves dilation of stenotic pulmonary valves. Use of balloon angioplasty and valvoplasty, however, has also been extended to aortic valve stenosis [9], stenotic distal pulmonary arteries [10], and aortic coarctation [11].

One previous report described the use of a dissolvable suture to band the pulmonary artery but allow subsequent balloon angioplasty. In that study by Rocchini and associates [14], 2-0 Vicryl suture was used in place of a band and resulted in a mean systolic gradient of 59 ± 14 mm Hg. Balloon angioplasty resulted in a decrease of the gradient to 7 ± 2 mm Hg. A subsequent report by this group [15] indicated that the excellent relief of right ventricular outflow obstruction persisted at follow-up evaluation 6 months later.

Our results also demonstrated persistent relief of the obstruction 13 to 14 months after balloon angioplasty. However, restenosis with systolic gradients of 33 and 52 mm Hg developed in 2 animals. No data are currently available regarding the likely success of repeat angioplasty at the pulmonary artery band site nor is there any reliable way to predict if the pressure gradients would continue to rise with longer-term follow-up without repeat balloon angioplasty. However, we believe that because it was successful initially, repeat balloon angioplasty would likely result in subsequent relief of the obstruction. Furthermore, as the animals had achieved full adult size, worsening obstruction seems unlikely. The difference in results between our study and that of Meliones and co-workers [15] could be due to (1) the longer follow-up in this report, (2) differences in balloon angioplasty technique, or (3) differences between using actual band material versus a dissolvable suture.

Because our pathological results indicated that the segments of the band were detached from each other and lying within a fibrous capsule, it is reasonable to assume that repeat balloon angioplasty could be performed, with perhaps better results.

Whether an actual band is superior to a suture for optimal surgical intervention and subsequent balloon angioplasty remains to be seen. Further studies and clinical application with longer follow-up will be necessary to address this issue. In addition, only clinical application with long-term follow-up can answer the question whether balloon angioplasty at a pulmonary artery band site will obviate the need for surgical reconstruction.

In summary, the present study supports the concept of pulmonary artery banding that can be relieved nonsurgically with balloon angioplasty, thereby resulting in a marked reduction in gradient and right ventricular systolic pressure along with an increase in diameter of the pulmonary artery band site. Whether or not the trend toward increasing gradient and right ventricular systolic pressure recorded over the 14-month period after balloon angioplasty would continue can be answered by ongoing follow-up. Repeat balloon angioplasty may be helpful in alleviating stenosis in those instances in which increasing obstruction occurs late after the initial balloon angioplasty procedure.

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Morphology of Pulmonary Atresia With Intact Ventricular Septum in Patients Dying After Operation

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In 1976, we adopted staged surgical management of pulmonary atresia with intact ventricular septum: stage 1 = establishment of a systemic to pulmonary artery shunt; stage 2 = open reconstruction of the right ventricular outflow tract and pulmonary valve; and stage 3 = closure of the shunt and interatrial communication. The morphological features of nine specimens obtained from 10 patients who died were reviewed. Special attention was given to features that might have influenced the poor surgical outcome in these patients. Survival after stage 1 depends on adequate systemic to pulmonary artery blood flow, initially as a combination of ductus arteriosus and shunt flow, with subsequent modification if the ductus closes. After stage 2, survival is influenced by left ventricular function and mitral valve function. The success of final correction (stage 3) depends largely on the morphology of both ventricles and their atrioventricular valves. It appears that the behavior of the ductus arteriosus and the size of the shunt are of vital importance for the survival of the infant. In 3 of the specimens, no right ventricular outflow tract was present, and in 2 others, short chordal attachments of the mitral valve were observed. Staged surgical correction appears to be a satisfactory approach if these considerations are taken into account.

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The infant with pulmonary atresia and intact ventricular septum remains a challenge to clinicians [1, 2] and surgeons [2–4]. Only a few pathological investigations that have looked specifically into the anatomy as it relates to surgical options have been published [5, 6]. A "staged" surgical procedure was adopted for the operative management of these infants at the Royal Liverpool Children's Hospital in 1976. The philosophy of the approach is threefold. The first stage is to support the pulmonary circulation with a systemic to pulmonary artery shunt, which will also encourage the pulmonary arteries to grow. The second stage is to decompress the right ventricle by providing an outlet into the pulmonary circulation. This is achieved by reconstructing the right ventricular outflow tract (RVOT) and the pulmonary valve and annulus while the systemic to pulmonary artery shunt is maintained. It is hoped that growth of the right ventricle will follow. The third stage is to take down the systemic to pulmonary artery shunt and close the interatrial communication.

For the infant to survive these procedures, certain criteria have to be fulfilled. For stage 1 survival, it is mandatory that a patent atrial communication exist and that an adequate pulmonary blood flow be established. To survive stage 2, it is essential that both the left ventricle and the mitral valve function adequately. Satisfactory function of the right ventricle and the tricuspid valve is necessary to survive stage 3.

With these criteria in mind, the present study was carried out in an attempt to evaluate which anatomical features might have mitigated against a successful outcome at any of these stages.

Material and Methods

Between 1976 and 1986, 45 neonates or infants underwent a three-stage procedure for pulmonary atresia with intact ventricular septum at the Royal Liverpool Children's Hospital. Thirty-seven underwent a shunt operation (stage 1) before the age of 1 month, with seven hospital deaths. Stage 2 was performed in 26 patients, 22 of whom were less than 2 years of age. There were two hospital deaths, and both patients were operated on before they were 9 months old. Total correction (stage 3) was performed in 7 patients, 5 of whom were less than 2 years of age. One infant, who was younger than 9 months old at the time of operation, did not survive the procedure. In total, 10 patients died during their hospital stay. From these 10 patients, nine autopsy specimens were available for further studies. One specimen from a neonate who died after a stage 1 operation was not available for morphological examination.

Specimens

Each of the nine heart specimens was routinely fixed in 4% formaldehyde solution. The right and left ventricles were opened from the atrioventricular junction to the

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ventricular apex along the acute and obtuse margins, respectively. Particular attention was given to the integrity of the atrioventricular valves, the endocardium, and the myocardial wall. Each ventricle was opened from its apex into its outlet portion.

Measurements

The diameters of the tricuspid and mitral annuli, the descending aorta, the pulmonary trunk, and the right and left pulmonary arteries were assessed by calculating the average of the greatest and the smallest diameters taken from cross sections. The tables of Rowlatt and associates [7] showing normal values were used as reference.

The right ventricular inlet dimension was considered the distance between the internal apical point and the tricuspid valve annulus below the coronary sinus at the junction between the interventricular septum and the posterior wall of the heart. The right ventricular outlet was measured from the right ventricular apex to the most distal point in the RVOT. In heart specimens with Ebstein's anomaly of the tricuspid valve, the measurements were more complicated. The true right ventricular inlet measurement was made as described, and then the distance between the most distal point of tricuspid valve displacement and the right ventricular apex was measured. The difference between the two measurements was defined as the length of apical displacement.

Left ventricular inlet and outlet lengths were assessed by measuring the distances between the internal apical point and the mitral valve annulus at the junction between the interventricular septum and the posterior wall of the heart, and between the internal apical point and the nearest point of the aortic valve leaflet on the infundibular septum anterior to the central fibrous body, respectively.

Myocardial wall thickness was measured at three points in both ventricles: immediately underneath the tricuspid and mitral valves, at the ventricular apex of both the right and left ventricles, and in the outlet portion close to the site of the atresia and immediately underneath the aortic valve. Right to left ratios were calculated according to the method described by Zuberbuhler and Anderson [6]. In specimens with Ebstein's anomaly, the relative displacement of the tricuspid annulus was calculated as a percentage of the right ventricular inlet as follows:

(length of apical displacement/right ventricular inlet) × 100%

An overall index of myocardial wall thickness was calculated as a ratio by comparing the myocardial thickness at the apex with the average thickness of the myocardium at the inlet and outlet as follows:

thickness at apex/[(thickness at inlet + outlet)/2] × 100%.

Results

All specimens showed concordant atrioventricular and ventriculoarterial connections. The morphological findings are summarized in Table 1.

Table 1. Morphological Observations

	Tricuspid Valve												
Specimen No.	Ebstein's Anomaly	Dysplastic	Stenotic or Narrow Annulus	Imperforate	Right Ventricular Inlet to Outlet Ratio	Left Ventricular Inlet to Outlet Ratio	% Myocardial Thickness of Right Ventricle	% Myocardial Thickness of Left Ventricle	Endocardial Fibroelastosis	Abnormal Mitral Valve Chordae	Patent Ductus Arteriosus	Systemic–Pulmonary Artery Shunt	Atrial Septal Defect
Stage 1													
1	Yes	Yes	Yes	No	0.62	0.83	1.00	0.66	No	No	Yes	Yes	Yes
2	Yes	No	No	No	. . .[a]	1.00	1.50	0.59	No	No	No	Yes	Yes
3	No	Yes	Yes	No	0.74	1.00	2.52	0.84	No	No	Yes	Yes	Yes
4	Yes	No	Yes	No	. . .[b]	1.00	0.80	0.67	No	No	Yes	Yes	Yes
5	No	No	No	Yes	. . .[a]	0.89	2.00	0.71	Yes	No	Yes	Yes	Yes
6	No	Yes	No	No	0.73	0.95	0.77	0.67	Yes	No	Yes	Yes	Yes
Stage 2													
7	No	No	Yes	No	0.92	0.95	0.78	0.55	No	Yes	No	Yes	Yes
8	No	Yes	No	No	0.73	0.80	0.52	0.33	Yes	No	No	Yes	Yes
Stage 3													
9	Yes	Yes	No	No	0.76	0.86	0.85	0.67	Yes	Yes	No	No	No

[a] There was no right ventricular outflow tract in this specimen. [b] There was virtually no cavity in this specimen.

Stage 1 Specimens

A patent atrial communication was found in each of the 6 specimens. In two, a balloon atrial septostomy had been performed. A prominent valve of the inferior caval vein was present in two hearts. In all specimens, the tricuspid valve and mitral valve diameters were smaller than the mean values for normal hearts [7]. The ratio of the tricuspid valve diameter to the mitral valve diameter was smaller than expected for normal hearts. However, there was marked variability and an extensive overlap with normal values. Ebstein's anomaly was seen in 3 specimens, with annulus displacement of 13%, 25%, and 35%.

Right ventricular inlet, apical, and outlet portions were present in 3 hearts. In 2 hearts, no RVOT was found, but the inlet and outlet portions were partially identified. In one heart, the right ventricular cavity was virtually absent. The inlet to outlet dimension ratios as an indication of right ventricular cavity size are provided in Table 1.

The myocardium at the right ventricular apex was considerably thicker than the mean of the inlet and outlet because of crowding of the hypertrophic apical trabeculations. In 4 of the 6 specimens, right ventricular hypertrophy was considered to be present (percentage greater than 1.0) (see Table 1). The pulmonary valves of the specimens either without a RVOT or with a diminutive right ventricular cavity showed marked commissural ridges up to the center of the valve. In three specimens with larger right ventricular cavities showing inlet, apical, and outlet components, the commissural ridges were present only at the periphery of the membranous pulmonary valve.

Pulmonary blood supply was through a patent Waterston shunt in all 6 specimens. The ductus arteriosus was patent in 5 hearts. In the heart with a closed ductus arteriosus, the diameter of the Waterston shunt measured 1 mm. In one specimen, the combined diameter of the Waterston shunt and the patent ductus arteriosus measured 3 mm and in two specimens, 4 mm. In the remaining two hearts, the combined diameters measured 5 and 8 mm. No systemic to pulmonary collateral arteries originating from the descending aorta were identified. Endocardial fibroelastosis of the right ventricle was present in two specimens.

Stage 2 Specimens

A patent atrial communication was found in both specimens. The tricuspid valve was very narrow in one and dysplastic in the other. Right ventricular cavity size expressed as the ratio of inlet dimension to outlet dimension (see Table 1) or as the right to left ratio was close to normal. Myocardial wall thickness at the right ventricular apex was also nearly normal.

As a result of RVOT reconstruction, the morphology of the right ventricle and the pulmonary valve could no longer be evaluated. In both specimens, the pulmonary blood supply was through a patent Waterston shunt of 2 and 3 mm. The ductus arteriosus had closed spontaneously in both hearts. There were no systemic to pulmonary collateral arteries originating from the descending aorta. Endocardial fibroelastosis of the right ventricle was present in one specimen. The mitral valve was supported by short chordae in one heart.

Stage 3 Specimen

The 1 specimen showed Ebstein's anomaly (10% displacement) of a dysplastic tricuspid valve. Right ventricular cavity size expressed as the inlet to outlet dimension ratio (see Table 1) and as the right to left ratio was close to normal. Endocardial fibroelastosis was present in the right ventricle. The mitral valve had short chordae tendineae.

Comment

Pulmonary atresia with intact ventricular septum accounts for a small percentage (1% to 3%) of all congenital heart malformations in most clinical series [8–10]. Most neonates are seen within the first few days of life with extreme cyanosis. Without prompt surgical intervention, they usually die within a short time, although survival into later childhood or even adulthood has been reported [11–13].

A three-stage surgical approach was used in 45 neonates or infants. There were 10 hospital deaths, and the hearts from 9 of these patients form the basis of this study. Although an autopsy study inevitably includes the worst end of the spectrum of such an anomaly, we think it can throw light on potential surgical problems and management.

Table 2 shows the theoretical requirements necessary for a successful staged procedure in relation to the relevant pathology found after each of the three stages at postmortem examination. Neonates with pulmonary atresia and intact ventricular septum can survive only when a patent atrial communication is present, as this is the only outlet for the systemic venous return and a source of pulmonary blood flow through a patent ductus arteriosus. The atrial outlet appeared adequate in all patients.

After the shunt procedure (stage 1), survival depends on the magnitude of the pulmonary blood supply, which then consists of the combined flow through the ductus arteriosus initially and the shunt. In one specimen, the ductus arteriosus had closed spontaneously, and the Waterston shunt appeared to be too small. In another specimen, the systemic to pulmonary shunt in combination with the patent ductus arteriosus appeared inadequate. This neonate probably died of a lung infection. In three other specimens, the shunt appeared to be too generous. These conclusions are based on pathological observations. However, no corresponding clinical correlation is available. At present, the shunt of first choice is a modified Blalock-Taussig shunt. With this type of shunt, no size-related problems should be encountered.

There was great variation in the size of the right ventricle judged at stage 1. Only 33% of the hearts were considered to be normal in size, and about 17% were moderately hypoplastic and 50%, severely hypoplastic. The size of the tricuspid valve was usually proportional to the size of the ventricle, and anomalies of the valve itself

Table 2. Theoretical Requirements and Autopsy Findings Influencing Survival After Each Surgical Procedure

Surgical Procedure	Theoretical Requirements for Survival	Relevant Autopsy Findings
Stage 1: shunt procedure	Patent atrial communication	Present
	Pulmonary blood supply—PDA in combination with shunt	Closed ductus arteriosus, shunt inadequate or too large
Stage 2: RVOT reconstruction	LV and MV function after extracorporeal circulation	Myocardial damage, MV regurgitation
	Pulmonary blood supply	All ductus arteriosus closed
	Adequately sized RV or outflow portion	Inadequately sized RV
Stage 3: closure of ASD + shunt takedown	RV and TV function	Small RV or endocardial fibroelastosis, Ebstein's anomaly
	LV and MV function	MV regurgitation

ASD = atrial septal defect; LV = left ventricular; MV = mitral valve; PDA = patent ductus arteriosus; RV = right ventricle or right ventricular; RVOT = right ventricular outflow tract; TV = tricuspid valve.

were frequent. To allow RVOT reconstruction, an adequately sized right ventricle is necessary.

After RVOT reconstruction (stage 2), survival is influenced by left ventricular function and mitral valve function. Our earlier experience suggested that a systemic to pulmonary artery shunt was required to support the pulmonary blood flow in the early period after stage 2 (reconstruction of the RVOT and pulmonary valve). In 1 of the patients, myocardial function was severely diminished, probably the result of inadequate myocardial protection, and in the other, left ventricular function was compromised by the presence of mitral regurgitation due to short chordal attachments. This patient could not be weaned from cardiopulmonary bypass.

All nine left ventricular cavities and aortic valves were of normal size and structure. Left ventricular wall thickness was normal. However, in two hearts (22%), the mitral valve was abnormal. The incidence of mitral valve pathology in pulmonary atresia and intact ventricular septum has not been evaluated in the literature. In the future, careful preoperative evaluation of mitral valve anatomy and function should be carried out in this group of patients.

After the establishment of continuity between the right ventricle and the pulmonary artery, an increase in right ventricular cavity size was measured, as is reported by other authors [2, 9].

After complete correction (stage 3), survival is influenced by the ability of the heart to regain adequate bilateral ventricular function. In the single specimen examined, we found Ebstein's anomaly of the tricuspid valve and severe right ventricular insufficiency due to a small right ventricular cavity in association with endocardial fibroelastosis. Moreover, the capability of the left ventricle to function well appeared reduced because of mitral regurgitation caused by short chordal attachments.

In all nine specimens, the tricuspid valves were abnormal in size and structure. Ebstein's anomaly was present in four specimens. In two specimens, the apical displacement was more than 20% of the right ventricular inlet length. In their series, Zuberbuhler and Anderson [6] reported a 14% incidence of normal tricuspid valves and a 27% incidence of Ebstein's anomaly. Seven of our nine specimens had a small or tiny right ventricular cavity. Hypertrophy of the right ventricular wall was observed in four specimens. No coronary artery fistulas were noticed either clinically or pathologically. The morphology of the RVOT could be evaluated only after stage 1, when RVOT reconstruction had not yet been performed. Three of those six hearts showed absence of any RVOT. In these 3 patients, open RVOT reconstruction as a second-stage procedure would have been contraindicated.

Pulmonary valve malformations in our series were related to the RVOT morphology. Domed valves were found only in association with an outlet component of the right ventricle [6, 14]. The main pulmonary artery was patent in all specimens, and the diameters of the main, right, and left pulmonary arteries related normally to each other.

In conclusion, based on our experience in the clinical management of neonates and infants with pulmonary atresia and intact interventricular septum over a 20-year period and this autopsy study, we suggest that a staged surgical approach can give satisfactory results provided the following factors are considered:

1. An adequately sized right ventricle with an adequate outlet portion is necessary to allow RVOT reconstruction.
2. Unless the ductus arteriosus is ligated at the time of creation of a systemic to pulmonary artery shunt or it closes spontaneously soon afterward, the combination of shunt flow and ductus flow could be excessive. The Waterston shunt may not be the shunt of choice in the management of this anomaly, as it is difficult to create to an "exact" size, and this could result in inadequate or excessive pulmonary blood flow. Four of six deaths after stage 1 were probably due to an inadequately sized shunt.
3. Adequate myocardial protection must be provided at the time of stage 2 RVOT reconstruction. Mitral valve anatomy and function should be evaluated preopera-

tively. Mitral regurgitation may have contributed to the death of 1 infant at the time of stage 2 reconstruction. The systemic to pulmonary artery shunt is usually still necessary after stage 2 reconstruction to initially support an inadequately functioning right ventricle.

4. Adequate function of the left and right ventricles and the atrioventricular valves is necessary for survival after stage 3 (closure of interatrial communication and takedown of shunt). One death occurred in this group. The patient had a combination of Ebstein's anomaly, a small right ventricular cavity, a mitral valve abnormality, and endocardial fibroelastosis.

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New Approach to the Surgical Treatment of Swyer-James-MacLeod Syndrome

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Three patients with Swyer-James-MacLeod syndrome underwent operation. Occlusion of the main bronchus, leaving the lung in place, was carried out with good long-term results.

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Unilateral pulmonary emphysema or unilateral hyperlucent lung was first described by Swyer and James in 1953 [1]. In 1954, MacLeod [2] reviewed 10 cases of one-lung transradiancy and analyzed clinical, radiological, and bronchographic features of the disease in detail. The main radiological feature of the disease is hypertransradiancy of the lung and diminishing of its size. Diagnosis is based on (1) obliteration of the small bronchioles, (2) hypoplasia of the pulmonary artery and absence of the peripheral vascular bed, and (3) emphysema [3–5]. Most investigators believe that this syndrome occurs as a result of infective damage of airways after obliterating bronchiolitis in childhood [6]. Hypoplasia of lung vessels and emphysema are considered to be secondary to chronic inflammation [4, 5].

Chronic infection of the damaged lung is an indication for operation, usually pneumonectomy [2, 3]. We performed occlusion of the main bronchus by its resection, leaving the lung in place in 3 patients with Swyer-James-MacLeod syndrome. There were 2 female patients and 1 male patient aged 38, 42, and 23 years, respectively. All had had chronic pneumonia since childhood, with episodes of acute infection two to three times per year. From time to time hemoptysis developed. Both women had ankle edema, and their condition was moderately severe. Sputum production was less than or equal to 150 mL/day. Respiratory function was seriously disturbed. Their vital capacity was 37% and 42% of predicted, and residual lung volume was 200% and 250% of predicted. Airway resistance was four times more than predicted, and expiratory flow rates were decreased to 20% to 30% of predicted. Roentgenogram showed hyperlucency of the right and the left lungs. Computed tomography revealed emphysematous alterations of the affected lungs (Fig 1). Perfusion scintigraphy demonstrated the absence of blood flow in the damaged lungs. Angiography showed hypoplasia of the pulmonary artery and obliteration of the peripheral vascular bed (Fig 2). Owing to short disease history, the young man was doing better, and his respiratory function was less disturbed, although hemoptysis developed several times and he had repeated infection two times per year.

All patients underwent operation with the diagnosis of Swyer-James-MacLeod syndrome: in 1 woman, the left lung was affected; in the other 2 patients, the right lung was affected. Operative procedure was performed through a posterior thoracotomy without dissecting the lattissimus dorsi muscle. The fourth rib was resected subperiostally. The parietal pleura was exfoliated, and the main bronchus was dissected extrapleurally; 1.5 cm of bronchus was resected. The central part was stapled, and the peripheral part was closed by interrupted sutures with interposition of mediastinal pleura.

The postoperative period was uneventful in all patients, and they were discharged on the seventh, eighth, and tenth day after operation, respectively. The women were followed up for 3 and 3.5 years, respectively, and the man was followed up for 1.5 years. An excellent clinical effect of operation was noted. Hemoptysis and sputum production ceased. No infection developed. All patients gained weight. Respiratory function improved substantially in the women: vital capacity increased by 600 and 800 mL, respectively, residual lung volume decreased by 50%, expiratory flow rates increased by 30%, and airway resistance decreased by 50%. Computed tomography showed fibroatelectasis of isolated lungs, displacement of the mediastinum toward occlusion, and herniation of the lungs to the contralateral pleural space (Fig 3). During exercise, oxygen saturation did not change and was maintained at a level of 80 to 85 mm Hg in arterial blood. The man had no improvement in respiratory function because he was in the early stage of disease and his lung function was not decreased initially; however, he became completely asymptomatic.

Comment

The effect of occlusion of the main bronchus is identical to pneumonectomy. Occlusion is less traumatic, and the operation is performed through a small thoracotomy without entering the pleural space. Occlusion of the main bronchus in these patients is directed at preserving the functional systems, especially in severely ill patients. The remaining lung acts as a biological prosthesis and diminishes mediastinal displacement and subsequent hyperexpansion of the other lung. Use of bronchoscopy to elimi-

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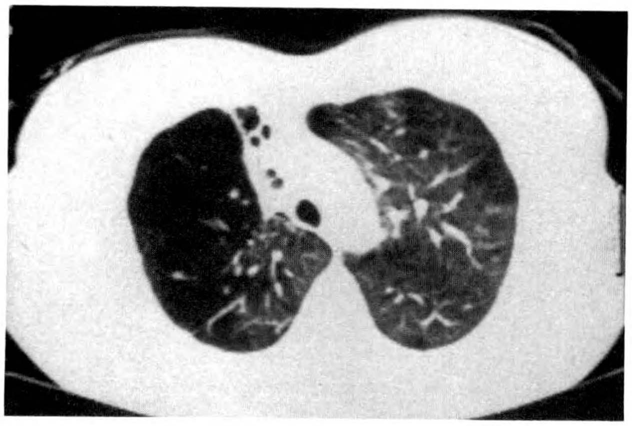

Fig 1. Computed tomography of the thorax before operation shows hypertransradiancy of right lung: emphysema.

nate sputum from the bronchial tree and of antibiotics against aerobes and anaerobes administered before and after operation in high doses avoids the complications of infection. If infection does not occur postoperatively or during the first year after operation, it should not be expected further, because experiments show that in 2 years after occlusion of the bronchus, fibroatelectasis of lung parenchyma develops and inflammatory changes in bronchus and lung tissue cease [7].

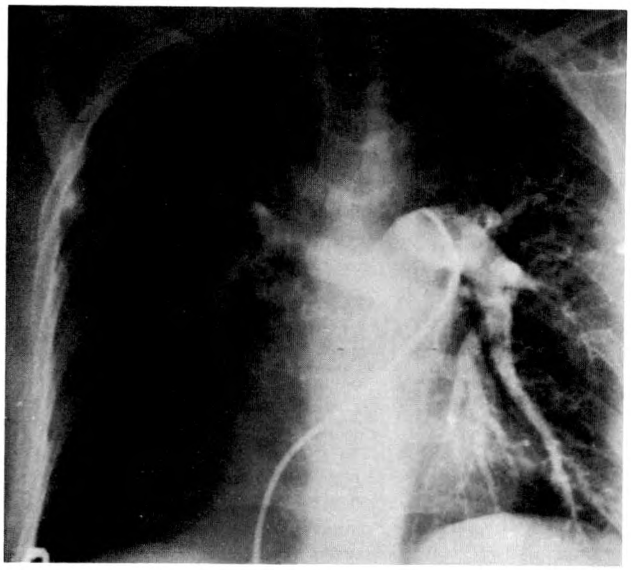

Fig 2. Angiography of the same patient as in Figure 1 before operation shows hypoplasia of right pulmonary artery and obliteration of the peripheral vascular bed.

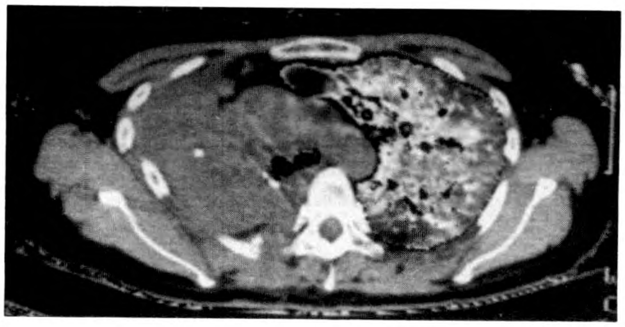

Fig 3. Computed tomography of the thorax of the same patient as in Figures 1 and 2 2.5 years after operation shows fibroatelectasis of the right lung; density is 52 H.

After a long-term period of segmental and lobar bronchus resection for management of bronchiectasis, functional occlusion of lung vessels was shown to develop [7]. Nevertheless, there is no doubt that occlusion of the bronchus in patients with normal lung vessels will produce massive V/Q mismatch, shunting of blood "right to left," and hypoxemia. Therefore, we believe that occlusion of the main bronchus, leaving the lung in place, can be used for management of Swyer-James-MacLeod syndrome when there is no blood flow to the affected lung. We also believe that occlusion of the main bronchus is effective in management of pulmonary artery agenesia and atresia.

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Critical Aortic Stenosis in the First Month of Life: Surgical Results in 26 Infants

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Between 1980 and 1989, 26 infants aged less than 1 month underwent open aortic valvotomy for critical aortic stenosis. All had congestive heart failure requiring inotropic agents (58%), ventilation (42%), and/or prostaglandin E_1 (35%) preoperatively. Nine patients with isolated aortic stenosis had an operative mortality of 0%, whereas 17 patients with other anatomical lesions had a 47% mortality ($p < 0.01$). Univariate analysis failed to identify additional risk factors other than year of operation ($p < 0.05$). There were four late deaths, three probably related to arrhythmia (actuarial survival at 113 months = 0.53). Two patients have required late reoperation; neither required valve replacement.

(Ann Thorac Surg 1990;50:105–9)

Critical aortic stenosis (AS) in the newborn continues to challenge the medical/surgical team. Although results worldwide have improved, substantial morbidity and mortality are still associated with the various surgical techniques in use [1–8]. We analyzed our own 10-year experience using one surgical technique. The factors affecting long-term and short-term outcome in the current era were examined. Our protocols and their shortcomings for diagnosing and treating critical AS in the newborn are discussed.

Material and Methods

Patient Population

During the period of this study, 152 children underwent aortic valvotomy at the Royal Children's Hospital (3% of all cardiac procedures). We excluded from consideration all patients aged more than 30 days at the time of operation. We believe, as do others, that the duct-dependent physiology, usual preoperative condition, and tolerance to cardiopulmonary bypass of the newborn differ from those of older patients [4, 9]. There were therefore 26 infants in this series, with a mean age of 8.7 days and a mean weight of 3.2 kg. All patients had serious congestive heart failure requiring inotropic support (58%), ventilation (42%), and/or administration of prostaglandin E_1 (PGE_1) (35%) preoperatively. The diagnosis was usually made clinically and confirmed with two-dimensional echocardiogram alone (22/26) or cardiac catheterization plus echocardiogram (4/26). Mean Doppler-derived or directly measured left ventricle to aortic gradient was 59 mm Hg (standard deviation, 15 mm Hg). Associated anatomical lesions including persistent ductus arteriosus (PDA) are shown in Table 1. We considered PDA a relatively constant hemodynamic feature of newborns with critical AS, and because our practice is to ligate the duct in all cases, it was not considered an additional lesion. Furthermore, all patients would currently receive PGE_1 preoperatively to maintain ductal patency. Recognizing the continuum of left heart obstructive lesions, we have excluded from this series patients with aortic atresia, mitral atresia, or both, for whom aortic valvotomy as primary treatment would not have been appropriate. Such patients were treated with various modifications of Norwood's operation, and results will be analyzed in another article. All patients admitted with critical AS survived to undergo open aortic valvotomy, which was the only procedure used during this period for this congenital lesion.

Surgical Techniques and Anatomical Finding

For patients whom we judged to have adequate-sized left ventricles and in whom aortic valvotomy was deemed to be the method of choice to relieve left ventricular outflow obstruction we used cardiopulmonary bypass, systemic hypothermia (30° to 32°C), and 4°C crystalloid cardioplegic arrest. A single right atrial cannula was used for venous return. The ductus arteriosus was routinely ligated after cardiopulmonary bypass was started. The aortic valve and subaortic area were inspected through an oblique aortotomy. Twenty-two of 26 patients had a bicuspid valve, 3 had a tricuspid valve, and 1 had a unicuspid valve. Only identifiable commissures were incised to the annulus to make the orifice as large as possible. When present, dysplastic nodules or excrescences on the leaflet edges were resected to decrease the bulk obstructing the orifice and to improve mobility and coaptation.

The bypass and operative techniques were modified as required to perform the concomitant procedures shown in

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Table 1. Lesions Associated With Critical Aortic Stenosis in 26 Infants

Lesion	No. of Patients
Patent ductus arteriosus only	9
Coarctation	6
Atrial septal defect	6
Ventricular septal defect	2
Mitral stenosis	6
Aortic annulus less than 5 mm	2
Hypoplastic left ventricle	3

Table 2. Of the last 3 patients shown in Table 2, 2 were initially treated with aortic valvotomy and could not be separated from cardiopulmonary bypass owing to inadequate size of the left ventricle. Atrial septectomy, proximal aortopulmonary window, and distal pulmonary artery banding were performed. The third patient underwent Gore-Tex innominate to right pulmonary artery shunt plus proximal pulmonary artery to aortic end-to-side anastomosis with division and patch closure of distal pulmonary artery, plus atrial septectomy. None of these patients survived the immediate postoperative period. Patients with this anatomy currently would be treated primarily with Norwood's operation and would not be considered for aortic valvotomy as a definitive procedure.

Of the 6 patients with coarctation, 1 had repair before aortic valvotomy, 2 had repair as a concomitant procedure, and 3 had repair as a second procedure during the same hospitalization (the diagnosis of coarctation was made after aortic valvotomy). Five other patients required reoperation in the immediate postoperative period, 1 for ventricular septal defect closure, 1 for modified Konno operation (after valvotomy failed to relieve the annular obstruction), 1 for mitral valve replacement, 1 for revision of a pulmonary artery band, and 1 for valvoplasty to reduce aortic insufficiency.

All patients were kept sedated, paralyzed, and ventilated for 12 to 24 hours or longer as required, during which time right and left atrial and pulmonary artery pressures were monitored. All patients operated on after 1985 had peritoneal dialysis catheters inserted at the time of operation for control of postoperative fluid and electrolyte balance and temperature. During the last half of this study, lignocaine infusion was started intraoperatively and maintained until the babies could be converted to oral phenytoin, which was then continued for 6 months postoperatively.

Follow-up

Follow-up for 1 to 113 months (mean, 37 months) after discharge was available for all hospital survivors in this study. Postoperative data were collected by us or by our referring cardiologists. All patients living in our own state were examined in our institution. For out of state or overseas patients, information was obtained from the referring cardiologist responsible for the child's long-term care.

Statistical Analysis

Characteristics of the subjects in the study were compared using Fisher's exact, χ^2, or t tests for discrete or continuous data as indicated. Actuarial data were calculated using the Kaplan-Meier formulas [10]. Sample proportions are expressed with confidence limits corresponding to one standard deviation with continuity corrections for upper and lower limits [11].

Results

Early Outcome

Overall operative mortality was 8/26 (31%; confidence limits, 21% to 45%). The babies with isolated AS with or without PDA had an operative mortality of 0/9 (0%; confidence limits, 0% to 19%). The patients with complex

Table 2. Operations Performed Concomitantly or During Same Hospitalization as Aortic Valvotomy

Operation (in Addition to Aortic Valvotomy)	No. of Patients	Hospital Deaths	Late Deaths
1 PDA ligation only	11	1 (low cardiac output owing to hypoplastic MV)	3
2 Coarctation repair	2	0	0
3 Coarctation repair + ASD closure	2	0	1
4 Coarctation repair + VSD closure	1	0	0
5 Coarctation repair + ASD/VSD closure	1	0	0
6 MV repair	1	1 (unable to wean from CPB)	. . .
7 MV replacement	1	0	0
8 ASD closure	3	2 (hypoplastic MV, arrhythmia)	0
9 Konno operation	1	1 (low cardiac output)	. . .
10 Hypoplastic left heart operation	3	3 (low cardiac output)	. . .

ASD = atrial septal defect; CPB = cardiopulmonary bypass; MV = mitral valve; PDA = patent ductus arteriosus; VSD = ventricular septal defect.

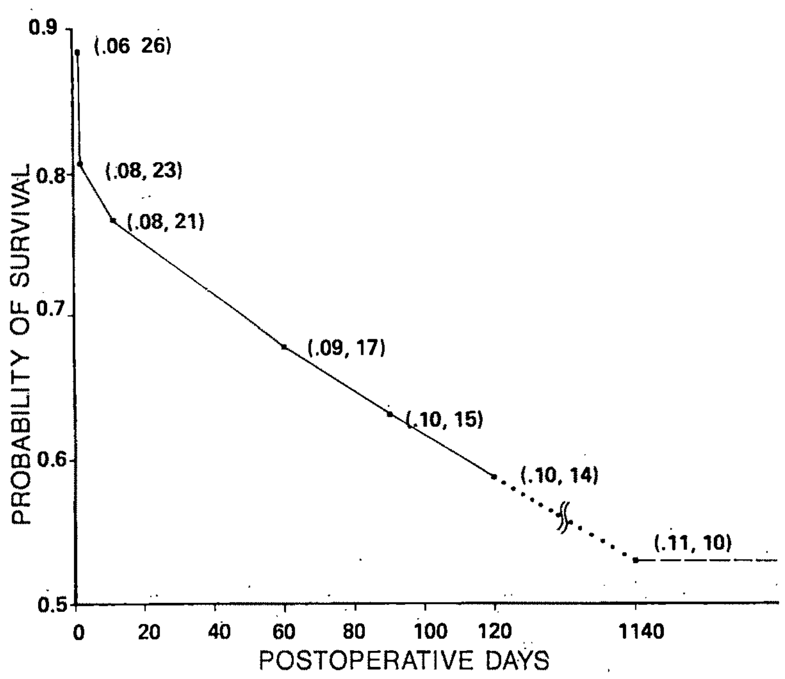

Fig 1. Actuarial survival after aortic valvotomy. Standard deviations of probability estimates and number of patients completing each follow-up interval are shown in parentheses.

AS had an operative mortality of 8/17 (47%; confidence limits, 39% to 62%). Details of early postoperative deaths are shown in Table 2.

Factors found to influence early mortality were presence of an additional anatomical lesion ($p < 0.01$) and operation before the last 2 years of the study ($p < 0.05$). Endocardial fibroelastosis (EFE) was identified by preoperative echocardiogram in 2 survivors and 2 nonsurvivors, but was detected postmortem in all 5 nonsurvivors undergoing autopsy.

Late Outcome

Follow-up of 1,194 patient-months after discharge disclosed four late deaths. Three patients had sudden death at home 2, 3, and 4 months after operation. These deaths were presumed to result from arrhythmias. One patient had initially undergone coarctation repair plus atrial septal defect closure plus aortic valvotomy and was hemodynamically well at evaluation 1 month before death on no medications. The second patient had isolated AS and was well just before death, receiving digoxin, furosemide, and phenytoin. Postmortem examination showed advanced EFE, although the AS was well relieved. The third late death occurred in a patient known to have severe EFE preoperatively. He was clinically well just before death, but autopsy showed a small dysplastic mitral valve in addition to the EFE. The fourth late death occurred during a bout of severe gastroenteritis 38 months after the original operation. Postmortem examination showed severe EFE. In the interim, this patient had required two reoperations for valvar and subvalvar AS although she had been asymptomatic. Postmortem examination showed severe EFE.

One other patient required reoperation 9 years after valvotomy. At the original operation, she had a dysplastic valve and underwent unicommisurotomy. At the second operation, four true cusps were noted, with minimal valvar stenosis but severe membranous and muscular subaortic stenosis. Her obstruction was successfully relieved by resection. Of the remaining survivors, 3 have mild aortic insufficiency and none has more than a 40-mm Hg transaortic Doppler-derived gradient.

Actuarial survival for all newborns with critical AS was 0.53 at 113 months (strictly speaking, at 38 months, with no deaths occurring after that time), as shown in Figure 1. The small number of late deaths does not lend itself to further meaningful statistical analysis except to indicate that hospital survivors with both complex and isolated AS are at risk.

Comment

Various surgical techniques for treatment of AS in critically ill newborns have been proposed. These include valvotomy under inflow occlusion [5], transventricular or transaortic closed valvotomy [1–3, 6, 7], and open valvotomy with cardiopulmonary bypass and aortic cross-clamping with or without cardioplegia [8, 12]. Hypothermic circulatory arrest with initial surface cooling has also been used [13]. Although comparisons of techniques in different institutions and heterogenous patient populations may be misleading, our technique compares favorably with other techniques for the group of patients with isolated AS.

Results with the more complex AS lesions have been less encouraging. Analysis of our own patients in this group suggests that at least six of the eight operative deaths occurred in patients with degrees of left heart hypoplasia more severe than valvar AS (small left ventricle, small aortic annulus, small mitral valve, subvalvar stenosis). The prognostic significance of preoperative left ventricular volume determination is controversial. Gundry and Behrendt [4] reported similar left ventricular end-systolic indexes for survivors and nonsurvivors in infants undergoing valvotomy for critical AS. Other investigators [14], however, have suggested that survival is unlikely with indexes less than 20 cm^3/m^2 [14].

Although we have not rigorously measured left ventricular volume in all cases, we currently consider size of the aortic annulus, ascending aorta, mitral valve, and left ventricular cavity when deciding which patients are suitable candidates for aortic valvotomy as initial treatment [8]. If the cardiac apex is not formed by the left ventricle, or if dimensions are less than 60% mean for body weight, we currently do not regard aortic valvotomy alone as appropriate treatment. This concept was not uniformly applied, however, in the earlier years of this series. Future results might be improved if all patients at this end of the spectrum could be identified with more certainty preoperatively and treated primarily with Norwood-type procedures or cardiac transplantation.

The exact incidence and degree of EFE in survivors is currently unknown. The high incidence and severity of this lesion at autopsy, however, suggests that some babies with complex AS and EFE might also be better candidates for cardiac transplantation than for aortic valvotomy (we have not yet performed transplantations for this indication).

Our current treatment protocol emphasizes noninvasive diagnosis and adequate resuscitation before operation [5, 14]. Although PGE_1 has been available since 1983 in our unit, it did not figure statistically in reducing operative mortality in the complex group. We do find PGE_1 to be an extremely useful resuscitation drug, however, and currently use it in all patients, as has been advocated by other investigators [15]. We also consider inotropic agents and ventilation important aspects of preoperative treatment in most patients, deferring operation until the baby is metabolically and hemodynamically more stable.

Regarding our surgical technique, we favor use of hypothermic (32°C) cardiopulmonary bypass with cardioplegic arrest. This technique allows a detailed inspection of the valve and a more precise repair than indirect techniques. Incising true commissures to the annulus provides a substantial increase in orifice size as compared with leaving 1 mm of fusion and does not lead to an appreciable increase in insufficiency. We also believe that debridement of the valve is important, especially if the configuration is trileaflet. Open repair makes this possible. In a bileaflet valve, a commissurotomy will usually lead to a substantial increase in orifice size, whereas a small trileaflet valve often has fairly well-developed commissures before valvotomy. In the latter case, debridement also allows further increase in orifice size without contributing to insufficiency.

Currently, we routinely close the foramen ovale through a small right atrial incision, using a very brief period of total circulatory arrest at 32°C. Associated mitral insufficiency of moderate degree is very likely to resolve after successful left ventricular decompression; in our experience, this does not require inspection or specific treatment at the time of valvotomy.

Postoperatively, we have found rapid atrial pacing to be useful in increasing cardiac output in infants with very hypertrophied left ventricles and relatively fixed stroke volume. We also have a low threshold for initiation of low-volume (10 mL/kg) peritoneal dialysis as adjunctive treatment for acidosis, renal insufficiency, electrolyte disorders, and hypothermia or hyperthermia.

The 3 sudden deaths at 2, 3, and 4 months, as well as some hospital deaths, are presumed to be related to arrhythmias. Because we have not observed complications attributable to long-term antiarrhythmic therapy, we currently use it for 6 months, recognizing that efficacy would be difficult to establish statistically.

We are aware that catheter balloon valvoplasty has been used successfully for treatment of newborn AS, although not in our own institution. As equipment and techniques improve, this procedure may be more widely and successfully applied. In our opinion it has not yet been proved to be superior to surgical treatment in either simple or complex newborn AS. The procedure is not free of complications, and long-term data are not available [16].

With regard to long-term follow-up, our data suggest that for survivors of the newborn period hemodynamically important residual AS and insufficiency are uncommon and not rapidly progressive during childhood. We presume that some of these patients will require repeat valvotomy or valve replacement later in life, because our longest follow-up is only 9 years.

We conclude that isolated AS in the newborn can be treated safely with open aortic valvotomy on cardiopulmonary bypass with the expectation of good medium-term results and low incidence of reoperation during childhood. Aortic stenosis complicated by other clinically significant hemodynamic lesions has a less favorable prognosis immediately after operation, but hospital survivors are likely to have medium-term results similar to those of patients with isolated AS.

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Aortic Valve Repair for Aortic Stenosis in Adults

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The stenotic aortic valve was surgically repaired in 48 adults, 21 women and 27 men, aged 38 to 83 years. Five had congenital aortic stenosis (AS), with a mean aortic valve gradient and area of 58 ± 23 mm Hg (standard deviation) and 0.54 ± 0.13 cm^2, respectively; 32 had senile AS with a mean aortic valve gradient and area of 43 ± 20 mm Hg and 0.98 ± 0.41 cm^2; and 11 had rheumatic AS with a mean aortic valve gradient and area of 59 ± 24 mm Hg and 0.47 ± 0.15 cm^2. Only 6 patients underwent isolated aortic valvoplasty, 11 underwent concomitant mitral valve procedure, and 34 underwent concomitant coronary revascularization. Repair consisted of decalcification in 33 patients and decalcification as well as commissurotomy in 15 patients. There were three hospital deaths, none related to the aortic valve. Only 2 patients (both rheumatic) did not improve clinically. During follow-up (mean, 64 ± 41 months) aortic valve restenosis developed in 24% (10 patients, 3/5 congenital, 4/11 rheumatic, and 3/32 senile) at a mean of 64 ± 28 months. Postoperative Doppler echocardiographic assessment of 21 patients with senile AS at 1.1 ± 2.7 and 18.1 ± 1.4 months showed significantly lower aortic valve gradient and improved area in comparison with preoperative values. At 36 ± 2.7 months, aortic valve gradient and area were not significantly different than preoperative values, and at 58.5 ± 2.6 months aortic valve gradient was 1.41 ($p = 0.07$) times the preoperative value. At 7 years, actuarial freedom from aortic valve-related symptoms of the patients with senile AS was 87%. We conclude that in select patients aortic valve repair results in excellent relief of AS. Late restenosis is expected and more likely to occur in the valves with congenital and rheumatic disease than in those with senile disease.

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During the 1950s and 1960s, debridement and commissurotomy were the only available procedures for relief of aortic valve stenosis [1–3]. These procedures, however, were recognized as "holding operations" [4, 5] rather than permanent solutions to the problem. Therefore, it is not surprising that as soon as the relatively efficient and more predictable prosthetic valve became available, replacement rather than conservation became the procedure of choice. Unfortunately, aortic valvoplasty was abandoned without a careful evaluation of the effect of factors such as severity of aortic valve stenosis and deformity, or etiology of the valvar disease, on the results. In view of the substantial morbidity associated with prosthetic valves [6, 7], identification of subgroups of patients suitable for aortic valvoplasty is important. A separate but related problem is whether aortic valvoplasty should be performed in patients referred for other cardiac operations who have associated aortic valve disease that is not severe enough to warrant a valve replacement but may degenerate further in subsequent years, necessitating cardiac reoperation.

With these issues in mind, our experience with surgical preservation of the aortic valve in 48 adult patients with aortic valve stenosis has been reviewed. Two main questions have been addressed in this study: (1) Is restorative aortic valvoplasty more feasible in certain subgroups of patients and does it offer adequate long-term results to warrant its application? (2) Can aortic valvoplasty result in prevention or retardation of progression of mild to moderate aortic stenosis?

Material and Methods

Patient Population

From January 1970 through January 1988, surgical repair of the aortic valve was performed in 48 adult patients, 21 women and 27 men, aged 38 to 83 years (mean age, 67 ± 12 years). Stenosis was the predominant aortic valve pathology in all patients. Eighteen patients had insignificant (2+ or less) aortic insufficiency. Mean New York Heart Association (NYHA) functional class was 3.1 ± 0.5. All patients underwent preoperative cardiac catheterization. Only 6 underwent isolated aortic valvoplasty; 6 (13%) underwent concomitant mitral valvoplasty, 31 (65%) underwent coronary revascularization, 3 (6%) underwent mitral valvoplasty and coronary revascularization, and 2 (4%) underwent mitral valve replacement. The aortic valve disease was the primary indication for operation in 34 patients (71%), whereas in the remaining 29% it was only a secondary objective for operation.

The patients were classified into three groups based on history, clinical data, and intraoperative visual examination: those with congenital bicuspid aortic stenosis, those

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Table 1. Congenital Bicuspid Aortic Stenosis

			Preoperative Catherization					Recatheterization			
Patient No.	Age (yr)	Sex	AV Gradient (mm Hg)	AV Area (cm^2)	AV Regurgitation	Operative Procedure	Symptomatic Relief (mo)	Months Since AV Repair	AV Gradient (mm Hg)	AV Regurgitation	AV Replacement (Months Since Repair)
1	57	M	40	0.51	1+	Decalcification	72	91	100	1+	92
2	38	F	60	0.36	0	Decalcification, commissurotomy	55	66	85	1+	67
3	60	F	84	0.52	0	Decalcification, commissurotomy	144	1st–48 2nd–138	25 50	1+ 1+	Never replaced
4	35	M	78	0.61	1+	Decalcification, commissurotomy	108	120	85	1+	120
5	70	M	30	0.70	0	Decalcification, CABG	3[a]	Never			

[a] Died of cerebral infarct.

AV = aortic valve; CABG = coronary artery bypass grafting.

with senile or degenerative calcific aortic stenosis, and those with rheumatic aortic stenosis.

BICUSPID AORTIC STENOSIS. The first group was composed of 5 patients (9%), 2 women and 3 men, aged 35 to 70 years (Table 1). All had moderate to severe aortic stenosis. The aortic valve gradient and area were 58 ± 23 mm Hg and 0.54 ± 0.13 cm^2, respectively.

SENILE AORTIC STENOSIS. The second group consisted of 32 patients (67%), 10 women and 22 men, aged 45 to 86 years (mean age, 70 ± 9 years) (Table 2). Average aortic valve gradient and area were 43 ± 20 mm Hg and 0.98 ± 0.41 cm^2, respectively. Thirty patients had serious coronary artery disease; 2 had serious mitral regurgitation. Two subgroups were identified. In the first subgroup (n = 14, asymptomatic aortic valve), the only presenting symptom was angina pectoris; the aortic valve gradient (peak to peak) was less than 40 mm Hg (mean, 26 ± 8 mm Hg), and the aortic valve area was larger than 0.9 cm^2 (mean, 1.4 ± 0.33 cm^2). In these patients, the primary indication for operation was coronary artery disease, and correction of aortic valve pathology was only a secondary objective. The patients in the second subgroup (n = 18, symptomatic aortic valve) had aortic valve-related symptoms: 4 had syncope or presyncope, 12 had congestive heart failure, and all had chest pain. The aortic valve gradient in these patients was 35 mm Hg or greater (mean, 55 ± 15 mm Hg), and the aortic valve area was smaller than 1.1 cm^2 (mean, 0.72 ± 0.17 cm^2). The primary indication for operation in these patients, besides coronary artery disease, was correction of aortic valve pathophysiology.

RHEUMATIC AORTIC STENOSIS. There were 11 patients (19%) in the third group, 9 women and 2 men, aged 42 to 79 years (mean age, 57 ± 12 years) (Table 3). Correction of aortic valve disease, alone or with coronary artery or mitral valve disease, was the primary indication for operation. The average (peak-to-peak) aortic valve gradient and area were 59 ± 24 mm Hg (range, 30 to 100 mm Hg) and 0.47 ± 0.15 cm^2 (range, 0.3 to 0.83 cm^2), respectively. All these patients had mitral valve disease. In 2 patients, the mitral valve disease was mild and did not require surgical intervention; in the remaining patients, average

Table 2. Senile Aortic Stenosis

				Preoperative Catheterization	
Status	No. of Patients	Mean Age (yrs)	Female/Male	Mean AV gradient (mm Hg)	Mean AV area (cm^2)
Symptomatic	18	74 ± 5[a]	10/8	55.2 ± 15.2[b] (range, 35–80)	0.72 ± 0.17[b] (range, 0.45–1.10)
Asymptomatic	14	66 ± 10	0/14	26.4 ± 7.7 (range, 15–40)	1.4 ± 0.33 (range, 0.9 ± 1.85)
All	32	70 ± 9	10/22	42.5 ± 19.8	0.98 ± 0.41

[a] $0.001 < p < 0.01$. [b] $p < 0.001$.

AV = aortic valve.

Table 3. Rheumatic Aortic Stenosis

				Preoperative Catheterization						Operative Procedure			
				AV			MV			AV		MV	
Group[a]	Patient No.	Age (yr)	Sex	Gradient (mm Hg)	Area cm^2	Regurg.	Gradient (mm Hg)	Area cm^2	Regurg.	Commis.	Decalc.	Commis.	MVR
A	1	47	F	80	0.48	1.5+	10	1.1	1+	+	+	+	
	2	61	M	55	0.50	0	0	. . .	0	+	+[c]		
	3	42	F	36	0.50	1+	10	0.8	1+	+	+	+	
	4	44	F	50	. . .	2+	14	. . .	1+	+	+	+	
	5	57	F	30	0.45	1+	15	1.0	2+	+	+		+
B	6	49	M	38	0.83	2+	16	1.2	1+	+	+	+	
	7	58	F	35	0.3	0	9	0.8	1+	+	+	+	
	8	79	F	56	0.47	0	8	1.4	2+	+	+		+
	9	74	F	86	. . .	2+	0	. . .	0	+	+[c]		
C	10	54	F	80	0.38	1.5+	20	0.8	1+	+	+	+	
	11	62	F	100	0.4	2+	12	1.2	0	+	+	+	
Total[e]		55.7 ± 11.6		58.7 ± 24.1	0.47 ± 0.15	1.5+	11.9 ± 4.4	1.0 ± 17	1+	n = 11	n = 12	n = 7	n = 2

[a] Group A experienced relief of AV-related symptoms throughout entire follow-up period, Group B experienced temporary relief of symptoms, Group C experienced no relief of symptoms. [b] = Doppler echocardiogram data [c] This patient had concomitant coronary revascularization. [d] This patient had a complication of a mitral Beall prosthesis. [e] Data are shown as mean ± standard deviation.

AV = aortic valve; AVR = AV replacement; Commis. = commissurotomy; Decalc. = decalcification; MVR = mitral valve replacement; Regurg. = regurgitation; W and A = well and alive.

mitral valve gradient and area were 12 ± 4 mm Hg (range, 5 to 20 mm Hg) and 1.0 ± 0.17 cm^2 (range, 0.8 to 1.4 cm^2), respectively. None of the patients had mitral valve regurgitation greater than 2+. Two had serious coronary artery disease.

Operative Procedure

Cardiopulmonary bypass with moderate systemic hypothermia was used in all cases. Myocardial protection was achieved by direct coronary perfusion until 1979 and by cardioplegic arrest thereafter. A left ventricular vent was inserted in all patients. The aortic valve was inspected, and if restoration of the cusps' mobility and coaptation appeared to be feasible, it was attempted. Calcium deposits were grabbed with a delicate rongeur or a Tonsil clamp and then carefully rotated and removed away from the elastic membrane. Our experience has shown that scoring the intima superficially at the border of plaques before removing them can prevent injury to the surrounding cusp tissue. Bits of calcium debris were removed with forceps or with a small metal sucker, which was very effective in scraping them off the elastic membrane. Fused commissures were divided sharply to within 1 mm of the annulus. Free debris was removed by copious irrigation and suction. In general, restoration was not attempted if there was extension of the calcifications to the ventricular aspects of the cusps, gross distortion of the normal architecture of the cusps, or extensive commissural fusion. After repair, valves were inspected to insure satisfactory mobility and coaptation, and the aorta was closed.

Competency was tested at the beginning of the operation and after closure of the aorta by estimating the volume of blood return through the left ventricular vent and by measuring the changes in systemic blood pressure during application and release of the aortic cross-clamp. A return of 10% to 15% or less of the total pump flow through the vent and a decrease in systemic blood pressure of 5 mm Hg or less when the aortic clamp was being released were considered satisfactory. A pulse pressure greater than 40 to 50 mm Hg while the patient was on complete cardiopulmonary bypass with a clamped vent was another helpful sign indicating clinically significant aortic valve regurgitation. Left ventricular and aortic pressures were measured simultaneously after the patient was weaned from cardiopulmonary bypass to assess the presence of residual gradient. Long-term anticoagulation and antiplatelet agents were not used.

Follow-up and Statistical Analysis

Follow-up was obtained during patients' office visits or from telephone interviews, charts, and the referring physicians. Endpoints of follow-up were death or aortic valve replacement or percutaneous valvoplasty. Percentage of follow-up was 98.8%, and the follow-up period ranged from 18 to 156 months (mean, 64 ± 41 months). Patients in whom symptoms developed underwent cardiac catheterization. More recently, two-dimensional and Doppler echocardiography was used for a noninvasive assessment of the valve area and gradient [8, 9] and to grade the regurgitation [10, 11] in all patients available for follow-

Table 3. (Continued)

Freedom From AV Symptoms (mo)	Recatheterization					Reoperation		Outcome
	Months Since Repair	AV		MV		Months Since Repair	Procedure	
		Gradient (mm Hg)	Regurg.	Gradient (mm Hg)	Regurg.			
148	125	5[b]	1+[b]	3[b]	1+[b]	Never		W and A, 148 mo
27	5	16[b]	0[b]	0[b]	0[b]	Never		Died of arrythmia at 27 mo
88	Never					Never		Died in accident at 88 mo
60	39	5	1+	14	1+	40	MVR	Died at 60 mo[d]
56	Never					Never		Died at 56 mo[d]
96	147	25	4+	12	1+	Refused		Died at 172 mo
52	70	90	2+	23	4+	Refused		Died at 106 mo
26	24	64	1+			Never		Awaiting AVR
48	53	0	3+	12	3+	53	AVR, MVR	Died during reoperation
None	10	60	3+	16	2+	12	AVR, MVR	W and A, 180 mo
None	25	76	1+	15	1.5+	25	AVR, MVR	Died during reoperation

up. Each of the 21 late survivors in the group with senile aortic stenosis underwent one or more echocardiographic examinations. Thirty-five studies were performed between 1 and 87 months postoperatively, 28 of which were done at 12 months or later. The ratios of the aortic valve gradients and areas at each point of time to baseline were calculated and grouped according to time intervals since repair (1 to 12, 12 to 24, 24 to 42, 42 to 72, and 72 months or longer). Because patients were evaluated at different times, changes in valve function over time were assessed by comparing the data at each of the time periods with baseline data by paired t test. The actuarial method was used for analysis of freedom from aortic valve-related symptoms. Because the numbers of patients in the bicuspid and the rheumatic groups were small, these groups were not analyzed separately. A p value less than 0.05 was considered significant. Values are expressed as mean ± standard deviation, unless indicated otherwise.

Results

Operative Results

BICUSPID AORTIC STENOSIS. All patients in this group had a successful valvoplasty and experienced relief of symptoms. All required decalcification; 3 required commissurotomy; 1 underwent concomitant coronary revascularization. There was no operative mortality.

SENILE AORTIC STENOSIS. Thirty patients in the senile aortic stenosis group underwent concomitant coronary artery revascularization, including repair of a left ventricular aneurysm in 2, mitral annuloplasty in 2, and carotid endarterectomy in 3. All were trileaflet valves. Eighty-four cusps (three cusps in 20 patients, two cusps in 12 patients) were debrided. In most patients, calcium deposits were primarily located at the aortic aspect of the cusps and were amenable to debridement. In three elderly patients, incomplete debridement was favored over valve replacement. In each of these patients, one of the three involved cusps had a calcium plaque that reached the ventricular aspect of the cusp, did not appear to affect mobility critically, and, if removed, would have resulted in a hole. The postdebridement gradient in these patients was less than 10 mm Hg. In 6 patients, a small (less than 2 mm) hole at the periphery of one cusp was created, probably where calcium deposits penetrated into the myxomatous layer of the cusps. The holes were oversewn with 6-0 Prolene suture (Ethicon, Somerville, NJ) without any untoward effect on subsequent results. Commissurotomy was performed in only 1 patient. A mean of 3.3 ± 1.2 coronary arteries per patient were grafted in the group with senile aortic stenosis.

Successful restoration of valve motion without serious insufficiency was achieved in all patients: the intraoperative postrepair valve gradient was 5.4 ± 4.8 mm Hg (range, 0 to 10 mm Hg), and the ratio of postoperative to preoperative gradient was 0.11 ± 0.1. Three patients (aged 72, 73, and 74 years) died in the hospital of mediastinal sepsis, bleeding duodenal ulcer, and atheromatous emboli originating from calcified ascending aorta with multiple organ involvement (including cerebral and coronary), respectively. Postoperative echocardiography showed a well-functioning aortic valve in all 3 patients. In 1 patient, respiratory failure developed owing to transient phrenic nerve paralysis, and another patient had a stroke. This last patient was in atrial fibrillation and underwent a concomitant mitral annuloplasty and was not anticoagulated. Both patients recovered completely. One patient

Table 4. Rerepair and Postrepair Senile Aortic Valve Gradient, Area, and Regurgitation[a]

Variable	Time Period (Mean Time) Preoperatively (n = 32)	Intraoperatively (n = 20)	1 to 12 mo (1.1 + 0.3 mo) (n = 7)	12 to 24 mo (18.1 ± 1.4 mo) (n = 11)	24 to 42 mo (36.0 + 2.7 mo) (n = 5)	42 to 72 mo (58.5 ± 2.6 mo) (n = 10)	Longer than 72 mo (86.87 mo) (n = 2)
Aortic valve gradient (mm Hg)	42.5 ± 3.8	5.4 ± 1.1	14.7 ± 3.8	25.0 ± 3.7	35.4 ± 4.1	39.4 ± 4.1	66; 80
Aortic valve area (cm^2)	0.98 ± 0.09	. . .	1.87 ± 0.28	1.62 ± 0.37	1.34 + 0.03	0.97 ± 0.08	1.26; 0.81
Aortic Insufficiency[b]	. . .	. . .	0.43 ± 0.26	1.09 ± 0.31	1.1 + 0.32	0.09 ± 0.21	1+; 1+

[a] All values are shown as mean ± standard errors. [b] Aortic insufficiency assessed on a scale of 0 to 4+.

did not improve after aortic valve repair because of mitral regurgitation, which was underestimated initially and was not addressed during the operation. During reoperation for mitral valve replacement 3 months later, the patient's aortic valve was found to be functioning well. The rest of the patients in this group were discharged in NYHA class 1.1 ± 0.4 ($p < 0.001$ versus preoperatively).

RHEUMATIC AORTIC STENOSIS. All patients in this group underwent aortic valve commissurotomy and debridement. Of the 9 patients with serious mitral valve disease, 7 underwent mitral valve commissurotomy and 2 underwent replacement. Concomitant coronary revascularization was performed in 2 patients. Intraoperative testing showed satisfactory repair in all patients: the aortic valve gradient was between 0 and 10 mm Hg, and insufficiency was never estimated as worse than mild. There was no operative mortality. One patient who underwent aortic and mitral valve repair and was not anticoagulated postoperatively sustained left hemiplegia, which eventually resolved. Except for 2 patients who did not improve clinically, all patients were in NYHA class II or less at discharge.

Follow-up

BICUSPID AORTIC STENOSIS. Mean follow-up in this group was 87 ± 57 months. One patient remained in functional class II at the age of 72 years, 12 years after repair, with a gradient of 50 mm Hg at 138 months. Three patients experienced symptomatic improvement during a follow-up period ranging from 4.5 to 9 years. Eventually, all had symptoms of aortic stenosis and underwent aortic valve replacement. One patient died 3 months after aortic valve debridement of a cerebral infarct due to severe bilateral carotid disease. At autopsy, the aortic valve cusps had excellent mobility and were coapting well.

SENILE AORTIC STENOSIS. Mean follow-up in this group was 54 ± 34 months. There were nine late deaths: six in the symptomatic subgroup and three in the asymptomatic subgroup. Eight of the 9 patients who died were between 73 and 83 years of age at operation, and death occurred between 14 and 96 months thereafter. None had any signs suggesting deterioration of the aortic valve, and the cause of death was not related to the aortic valve in any of them (3 died of myocardial infarction, 3 of multiple noncardiac medical problems, 2 of malignancy, and 1 during abdominal aneurysm resection).

The aortic valve gradient and areas at the five time intervals are shown in Table 4, and the ratios of postoperative to preoperative values are shown in Figures 1 and 2. At 1.1 ± 0.3 months and at 18.1 ± 1.4 months, the ratios of the postoperative aortic valve gradient to preoperative values were significantly less than 1 and the ratio of postoperative aortic valve area to the preoperative value was significantly greater than 1. At 36 ± 2.7 months, the ratios were not different from 1. At 58.5 ± 2.6 months, the aortic valve gradient and area were 1.41 ± (standard error) 0.18 ($p = 0.07$ versus 1) and 0.9 ± (standard error) 0.22 times the preoperative values. Only 2 patients were studied at 86 and 87 months. In both, the aortic valve gradient was 3.0 times higher than the preoperative value, and the aortic valve areas were 0.7 and 0.5 times the preoperative values. Dividing the group with senile aortic stenosis by the preoperative median aortic valve gradient, the patients with the higher preoperative aortic valve gradient were compared with those with the lower gradient. No correlation between the groups and rate of restenosis was found.

Three patients had signs of aortic valve restenosis occurring 34, 46, and 90 months after repair. Their gradients before repair (25, 28, and 56 mm Hg) were not higher than the mean group gradient. Subsequently, 2 underwent aortic valve replacement and 1 had a valvoplasty. At 7 years, 87% of the hospital survivors with senile aortic stenosis were free of aortic valve-related symptoms (Fig 3).

RHEUMATIC AORTIC STENOSIS. Mean follow-up in this group was 70 ± 51 months. Based on long-term outcome, three subgroups were identified (Table 3). Group A (n = 5) never required reoperation of the aortic valve. One patient is alive and well 12 years after operation. The other 4 patients died during follow-up, but death probably was not related to the aortic valve in any of them. One patient died suddenly 27 months after repair while engaged in sporting activities, probably because of arrhythmia. Another patient was killed in a car accident 7 years after operation while in functional class I. The deaths of

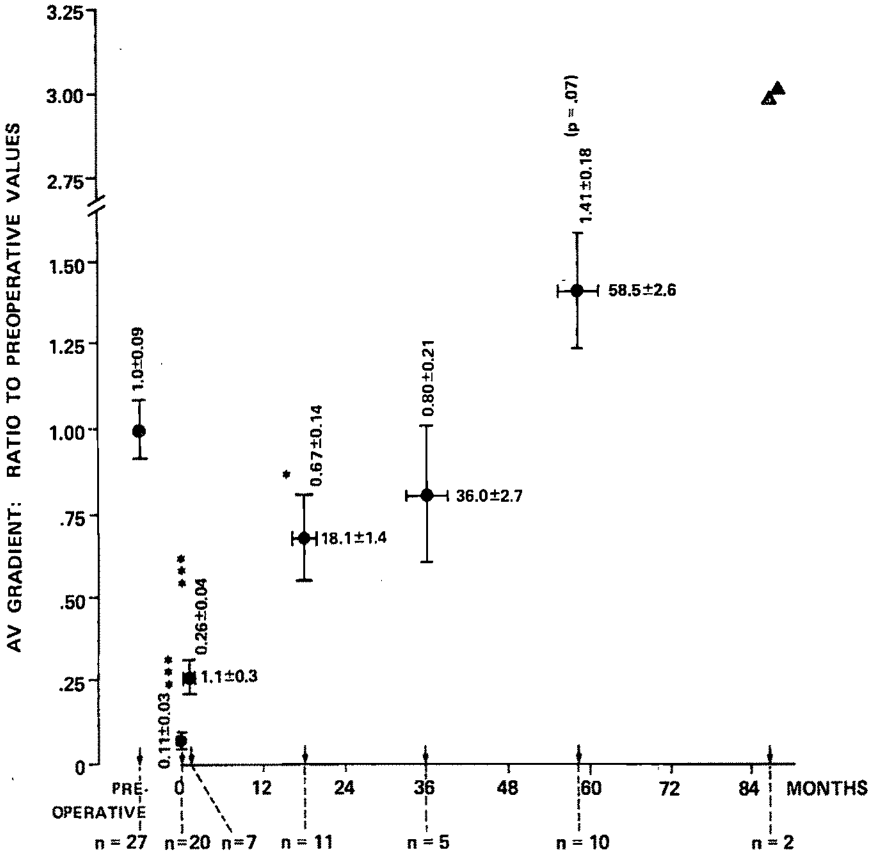

Fig 1. Ratios of postoperative aortic valve (AV) gradient to preoperative values at five postoperative time intervals. Values are presented as mean ± standard errors. (p = 0.05 to 0.01; ** p = 0.01 to 0.001; *** p = < 0.001.)*

the 2 other patients were attributed to a malfunctioning Beall valve prosthesis in the mitral position. In 1 patient, it was placed during the aortic valve repair operation; in the second patient, it was placed 14 months later. Three of these 5 patients underwent late cardiac catheterization that showed insignificant aortic valve disease. Group B (n = 4) experienced temporary symptomatic improvement that lasted between 26 months and 8 years. Two refused reoperation and died 9 and 14 years after repair. One died during reoperation, and 1 is awaiting aortic valve replacement. Group C (n = 2) did not experience postoperative symptomatic relief (Table 3, group C). Both underwent aortic and mitral valve replacement. One patient is alive and well; the other did not survive the reoperation. Mean aortic valve gradients of subgroups A, B, and C were 50 ± 20, 65 ± 13, and 90 mm Hg, respectively, but the differences were not significant.

THROMBOEMBOLIC EVENTS. Seven patients had cerebrovascular events. Only one event, however, could be related to the repaired aortic valve. It occurred in a patient with a bicuspid aortic valve who had amaurosis fugax 7 years after repair. In 4 patients, the cerebrovascular event was believed to be related to the mitral valve operation; one patient with a Beall mitral valve prosthesis had a fatal stroke after administration of warfarin was stopped because of bleeding complications; the other 3 patients had enlarged left atria and were in atrial fibrillation, under-

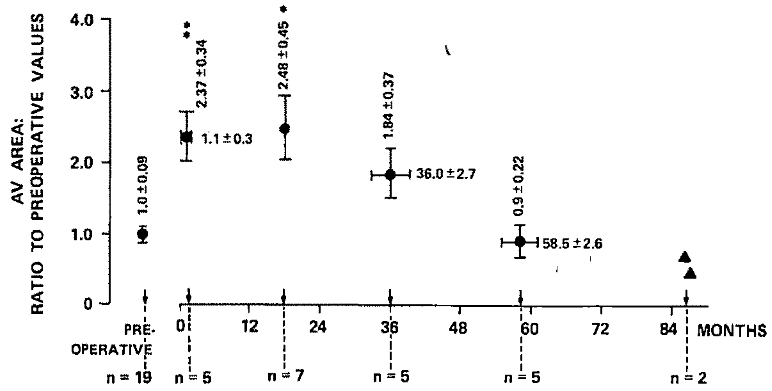

Fig 2. Ratios of postoperative aortic valve (AV) area to preoperative valves at five postoperative time intervals. Values are presented as mean ± standard errors. (p = 0.05 to 0.01; ** p = 0.01 to 0.001.)*

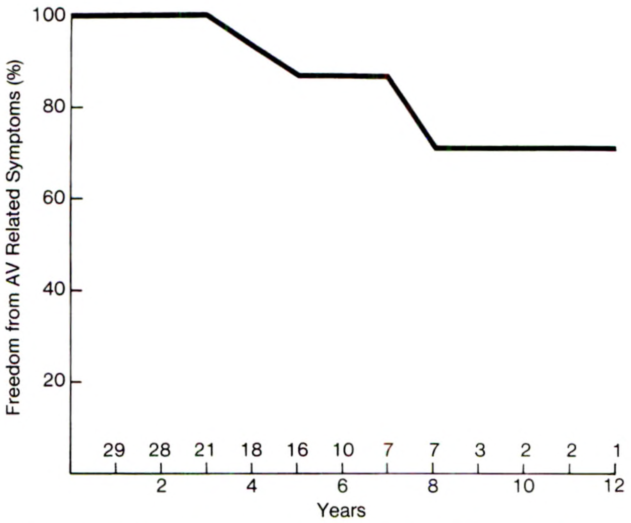

Fig 3. Actuarial freedom from aortic valve (AV)-related symptoms after AV repair in patients with senile aortic stenosis (n = 32). Numbers above the abscissa indicate number of patients entering each time interval.

went mitral commissurotomy or annuloplasty, and had nonfatal stroke. Two patients had fatal cerebral infarctions secondary to carotid artery disease. Excluding the last 2 patients and those with concomitant mitral valve disease, the linear incidence of thromboembolic events was 0.0062% per patient-year.

Histopathology

The debrided aortic valve was available for histopathological examination in 7 patients. Three were excised at 2, 4, and 10 weeks after debridement from patients who died of noncardiac causes. Gross inspection showed the valve leaflets to be pliable and well coapted, and the valve orifice was widely patent without commissural fusion. There was no evidence of thrombosis. Four valves were excised during aortic valve replacement; one was replaced 10 weeks after debridement (during mitral valve replacement, although the aortic valve was functioning well), and three were replaced at 53 months after debridement for aortic restenosis. Of the seven valves examined, only one (one of the three excised 53 months after debridement) was from the rheumatic aortic stenosis group and the rest were from the group with senile aortic stenosis.

A cusp explanted from a patient with senile aortic stenosis and not debrided is shown in Figure 4. At 2 weeks (Fig 5), the site where calcific material had been debrided was clearly apparent with a small amount of residual calcium. A second calcium plaque that reached very close to the ventricular aspect of the cusp was not debrided. At 10 weeks, the entire fibrosa layer was missing and the aortic surface of the cusp consisted of the elastica. A thick collagenous tissue was evident on the ventricular aspect of the myxoid zone (Fig 6). In the two valves with senile stenosis that were available 53 months after debridement, the cusps were denuded of the fibrosa layer, and calcified plaques appeared within the myxomatous layer (Fig 7). Sections of a rheumatic aortic valve received 53 months after debridement and commissurotomy showed extensive nodular calcifications and active fibrosis. Unlike in the valves with senile stenosis, none of the architectural features of the normal valve could be identified.

Comment

There has been a renewed interest in aortic valvoplasty, which may again become a suitable procedure in the modern adult cardiac surgical armamentarium. A few decades ago, repair of the aortic valve was the only available therapy for aortic stenosis. Unfortunately, the high incidence of late restenosis [3, 4, 12, 13] resulted in the disappearance of this operation when prosthetic valves became available. It soon became evident, however, that aortic valve replacement was not a cure and was associated with its own appreciable mortality and morbid-

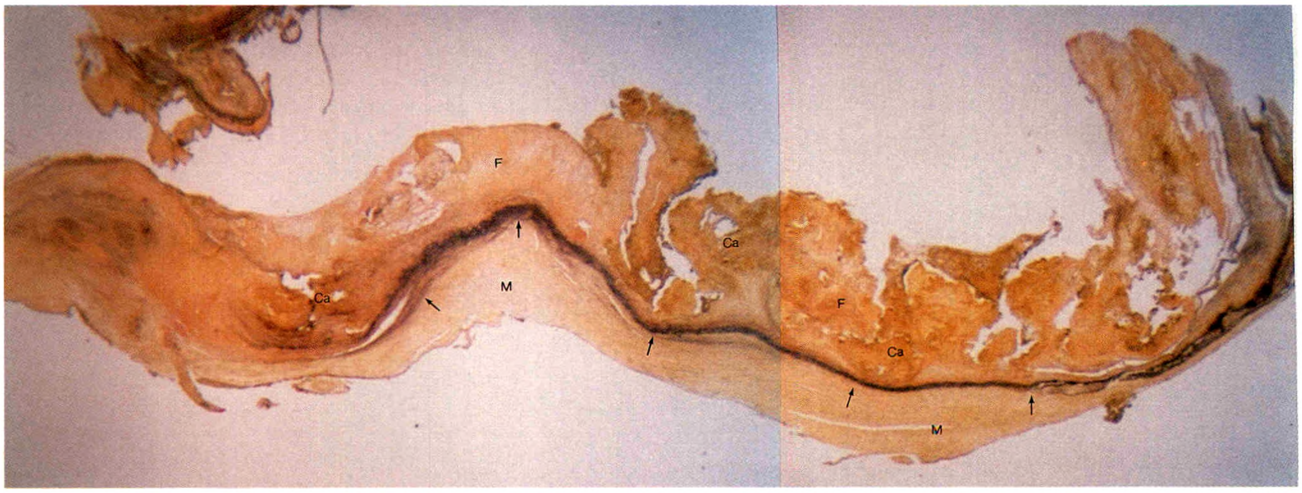

Fig 4. An undebrided cusp explanted from a patient with senile aortic stenosis. Calcium plaques (Ca) are confined to the aortic aspect, or the fibrosa (F) zone of the cusp, whereas the ventricular aspect, the myxoid (M) zone, is free of calcifications. The two zones are separated by the intact elastica (arrows). (Elastic stain, ×4 before 41% reduction.)

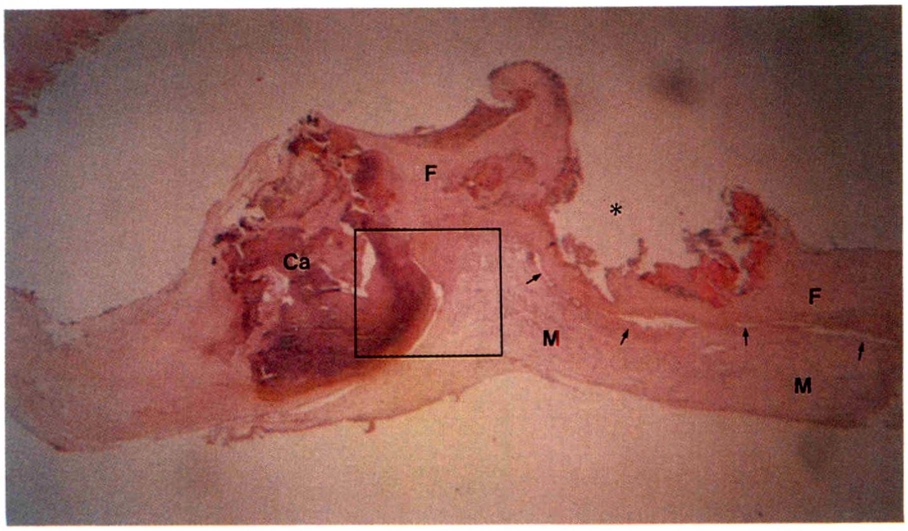

Fig 5. A cusp explanted 2 weeks after debridement. The site of removal of a calcium plaque is marked with an asterisk, *next to another plaque* (Ca) *located close to the insertion line of the cusp. (Hematoxylin and eosin, ×4 before 32% reduction.)* (F = *fibrosa zone;* M = *myxoid zone;* arrows *mark the elastica layer.)*

ity. Despite continuous efforts toward improvement of existing devices and development of new designs, the risks associated with prosthetic or tissue valves in the aortic position remained substantial, averaging approximately 4% to 6% per patient year [14–16]. Because of these risks and because of the long-term symptomatic relief offered by valvoplasty in a substantial percentage of patients (18% to 44%) [4, 5, 12, 13], there is a renewed interest in this procedure [17–20]. The availability of modern ultrasonic devices (Cavitron Ultrasonic Surgical Aspirator, Cavitron Surgical Systems, Stamford, CT) may make decalcification safer and more expeditious [18, 21] and is another reason for a potential increase of applicability of the procedure.

The normal aortic valve opens by the folding of the three cusps into their respective sinuses and closes by their falling back across the ventricular outflow. The cusps are prevented from prolapsing into the ventricle by their concave semilunar shape and by the overlap of their free edges [22]. When all three cuspid features, namely, mobility, concave shape, and overlap, can be restored or preserved, a well-functioning valve can be expected. Based on these criteria, aortic valve restoration was considered feasible in 48 patients.

The repair was successful in all but 2 patients (95.8%) and was not associated with any untoward events, including creation of incompetent valves. Despite this success rate, considering the 25% incidence of late valve degeneration requiring replacement and the evidence of silent gradual increase in aortic valve gradient, it has to be concluded that the procedure is palliative for many patients and cannot provide cure for all. The least favorable results were obtained in the rheumatic group; in 2 of the 11 patients the procedure was not successful, and in 4 of the remaining 9 patients signs of restenosis or incompetence developed and aortic valve replacement was required at a mean of 56 ± 29 months postoperatively. In 3 of the 4 long-term survivors in the bicuspid group, signs of restenosis developed and aortic valve replacement was required at 55, 72, and 108 months. The most favorable results were obtained in the senile group; the repair was successful in all patients ($p < 0.05$ as compared with 9/11 in the rheumatic group), and signs of late restenosis requiring intervention have occurred in only 3 patients (at 34, 46, and 90 months) ($p < 0.05$ as compared with 4/9 in the rheumatic group).

The pattern of calcium distribution and the presence or absence of commissural fusion characterize each of the disease processes [22, 23]. Rheumatic AV stenosis is characterized by fusion of all three commissures in the younger age group and by thickening and calcification of the cusps, resulting in the rigidity of the entire valve in the older age group. Senile aortic valve stenosis, on the other hand, results from fibrosis and calcium deposits at the base of the cusps along the flexion stress lines, affecting their hinge mechanism, without commissural

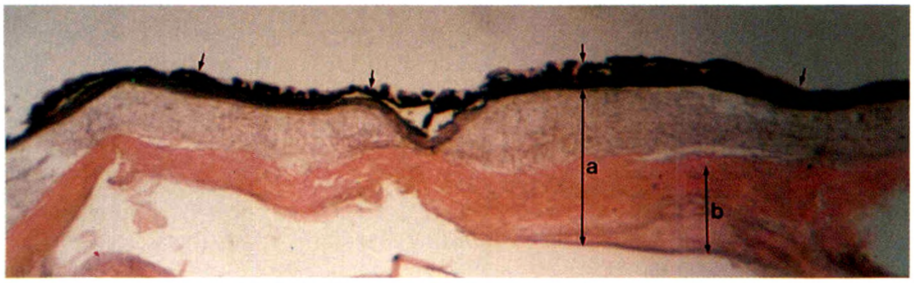

Fig 6. A cusp explanted 10 weeks after debridement. The entire fibrosa layer is missing, and the aortic surface of the cusp consists of the elastica (arrows). *The ventricular aspect of the myxoid zone* (a) *is replaced by collagenous tissue* (b). *(Elastic stain, ×4 before 31% reduction.)*

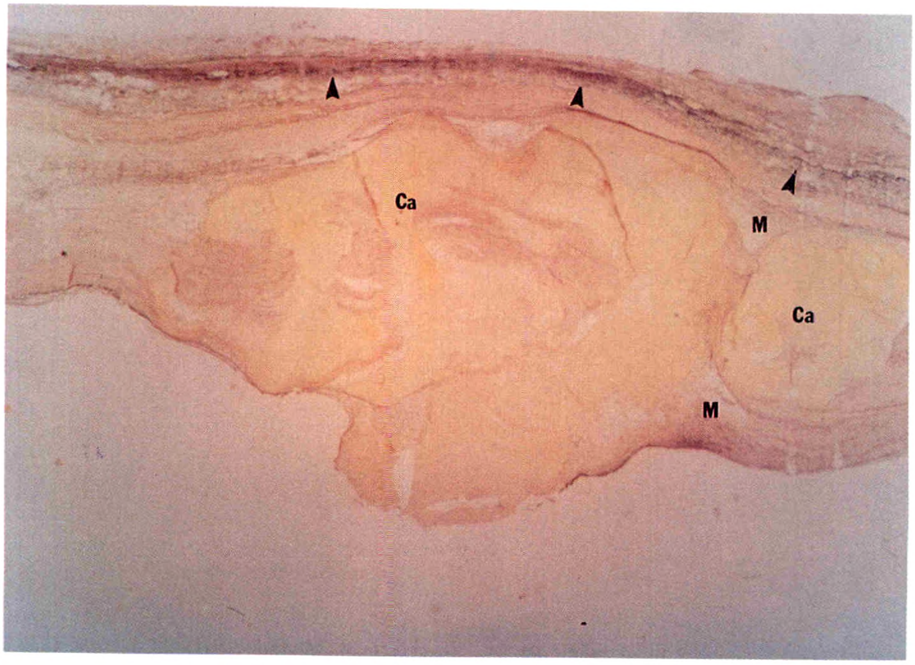

Fig 7. A cusp explanted 53 months after debridement because of restenosis. Restenosis appeared to be the result of neocalcifications (Ca) *within the myxoid layer* (M). *Arrows mark the intact elastica. (Elastic stain, ×4 before 32% reduction.)*

fusion (Fig 8). The stenotic bicuspid aortic valve is affected by a dystrophic process identical to the senile valve, but it occurs at a younger age. These differences in the pathological changes explain why the valves in the rheumatic and bicuspid groups had significantly more severe stenosis and were more severely deformed. It is not surprising, therefore, that we experienced a higher early success rate and more favorable long-term results in the senile valves, in which only the body of the cusps was involved, than in the rheumatic and bicuspid valves, in which the body and the commissures had to be repaired, as was the experience of Weinstein and colleagues [17], Mindich and associates [18], and King and co-workers [19]. A correlation between the preoperative aortic valve gradient and late restenosis cannot be demonstrated within any of the groups, which suggests that gradient per se does not represent the architectural changes of the valve and the severity of its deformity and, therefore, the feasibility of its repair. Although removal of all calcium plaques is desirable, occasionally it may be prudent to leave a plaque reaching the ventricular aspect of the cusp and not critical to its mobility untouched, and to accept a small residual gradient.

Analysis of the postrepair aortic valve hemodynamics at different times in the senile group showed return to prerepair gradient at 36 months and a gradient that was higher, although not quite significantly, than the prerepair value at 59 months. Some limitations in the methods of collecting this data should be appreciated, however. First, the Doppler-derived estimate of aortic valve gradient is modestly higher than the catheterization-derived gradient [8]. Because the Doppler-derived aortic valve gradient was not available preoperatively in most patients, the gradients after repair were compared with the preoperative catheterization-derived gradients; therefore, the calculated ratios are probably somewhat overestimated. Second, our data were collected, in part, retrospectively; therefore, they lack the advantage of serial longitudinal measurements. Third, 25% of the late survivors died free of aortic valve-related symptoms and were never studied postoperatively. Thus, in reality, the rate of restenosis may be lower than the figures cited. That the increase in aortic valve gradient was disproportionate to what would be expected by the relatively modest decrease in aortic valve area can probably be related to the postoperative improvement in left ventricular function. The 72% 7-year actuarial freedom from aortic valve-related symptoms of the entire population was not significantly different from the 87% calculated for the group with senile stenosis (Fig 9). We expect, however, that if the rheumatic and bicuspid groups were larger, such differences would probably be found. That only 3 patients in the senile stenosis group had symptoms consistent with aortic valve restenosis, and that a relatively high percentage were free of aortic valve-related symptoms at 5 years (87%), a percentage higher than would be expected by the rate of restenosis at the same time period, suggests that coronary artery disease contributed substantially to their preoperative symptomatology.

The availability of six senile valves excised at 2 weeks, 10 weeks, and 53 months after repair provided us the opportunity to study the postdebridement changes in these valves. Senile calcification begins in the fibrosa and most often is confined to this layer [22, 23] (Fig 4). Piece-meal removal of these placques (Fig 5) or stripping of the calcification-containing fibrosa (Fig 6) restores the hinge motion of the cusps and relieves stenosis. Once removed, the fibrosa does not appear to regenerate (Fig 7). Most interesting was the finding that restenosis appears to result from neocalcification in the myxoid zone,

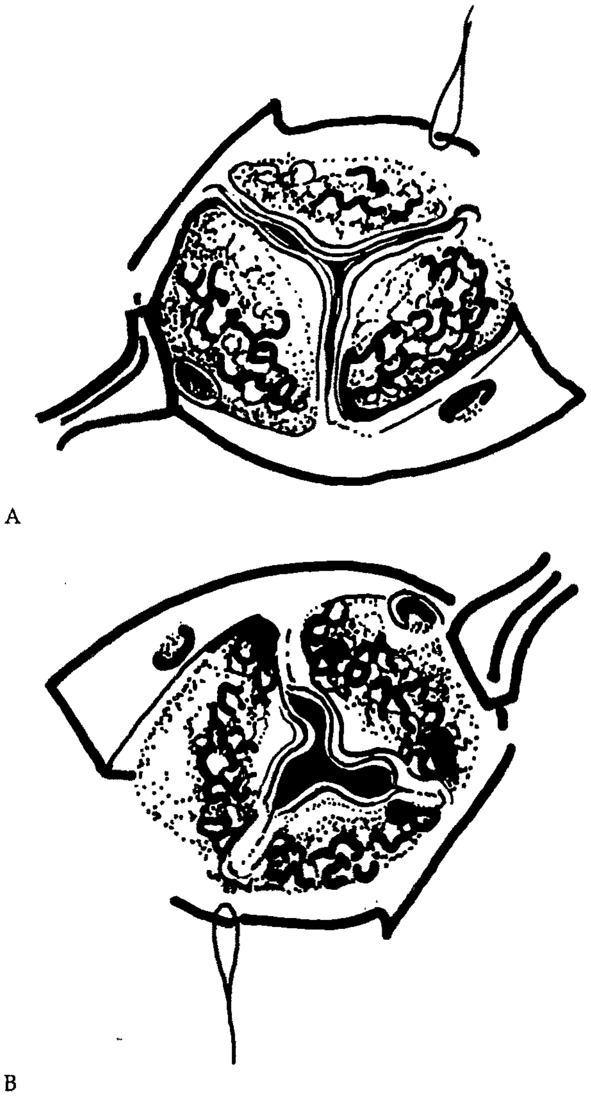

Fig 8. Pattern of calcium distribution and deformation of the senile (A) and rheumatic (B) aortic valves.

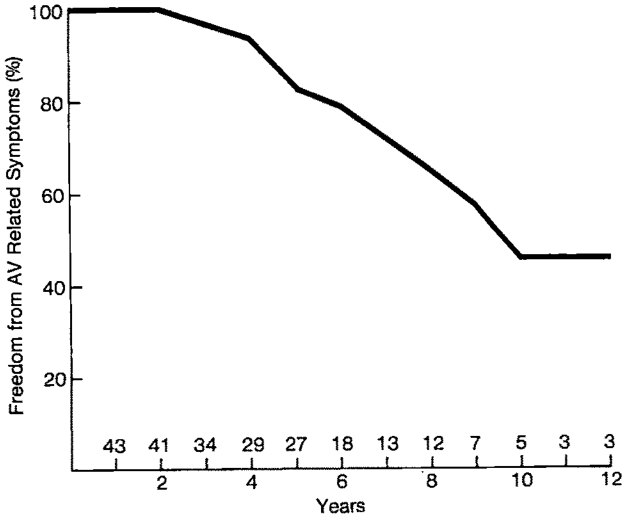

Fig 9. Actuarial freedom from aortic valve (AV)-related symptoms after aortic valve repair in the entire group (n = 48). Numbers above the abscissa indicate number of patients entering each time interval.

which was uninvolved before removal of the fibrosa. We speculate that the mechanical forces that normally are distributed between both the fibrosa and the myxoid layer are imposed solely on the relatively weak myxoid layer after debridement and promote fibrosis, which serves as a nidus for dystrophic calcification. Of interest is the relatively high incidence of aortic insufficiency (19%) occurring after debridement in some series [24] in which the ultrasonic technique was used; it was not used in our series, and an incompetent valve did not develop in any patient. We speculate that this may be related to the preservation of the elastica in all our patients, which may help prevent excessive fibrosis and resultant regurgitation. The low incidence of thromboembolic complications supports the policy of avoiding long-term anticoagulation after aortic valve repair.

Thirty-four patients (71%) were actually referred for advanced aortic valve disease, and aortic valve repair was an alternative to valve replacement. In 32 of these patients, valvoplasty was successful. The 6-year actuarial freedom from aortic valve-related symptoms was greater than 80%, and their native aortic valve was retained for a mean period of 66 ± 37 months. Considering the 3% to 5% annual rate of major prosthetic aortic valve-related complications [14–16], each of these patients was spared the cumulative risk of major complication—in the range of 15% to 25% if a prosthetic valve had been implanted. On the other hand, in a substantial number of patients (25% in our series), aortic valvoplasty is a palliative procedure and reoperation will be required eventually [3, 5, 12, 13]. The mortality rate for elective aortic valve reoperation is 1.5% [25]. Thus, if technically feasible, restoration should be considered because the benefit of sparing the patient the attendant risks of prosthetic or tissue valve replacement for the duration of palliation may outweigh the reoperation-associated risks.

Whether a diseased but asymptomatic aortic valve should be repaired or left untouched in patients undergoing operation for other cardiac problems is a more difficult dilemma and was relevant in the 14 patients who were referred for coronary revascularization but who also had mild to moderate aortic valve disease. Although the aortic valve was successfully repaired in all 14 patients (a preventive intervention), its merits should be judged not only in view of its technical feasibility and the associated low risk but also by its effect on the natural history of the disease. Progression of mild to moderate stenosis to a hemodynamically significant lesion has been reported. In a retrospective study, Cheitlin and co-workers [26] demonstrated progression of mild to moderate aortic stenosis in adults by an average increase of the aortic valve gradient of 1.3 mm Hg per month in 50% of patients. In a similar study, Wagner and Selzer [27] reported that in 40% of their patient population, the rate of decrease in the aortic valve area was 0.3 cm^2 per year. Employing a noninvasive scoring method, Nitta and associates [28] found in a prospective study that progression of aortic stenosis to a critical degree over a 3-year period occurred in 60% of patients.

The late follow-up of the 14 patients in our series with mild to moderate aortic valve stenosis suggests that progression of the disease has indeed been retarded by debridement. Only 2 patients (preoperative aortic valve gradient, 25 and 28 mm Hg) required aortic valve replacement 53 and 94 months after repair, and the other patients remained free from of aortic valve-related symptoms for a mean of 66 ± 38 months. However, the long-term value of this procedure in prevention or retardation of progression of aortic stenosis and its effect on the natural history of the disease should be evaluated further.

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Scimitar Syndrome: Cine Magnetic Resonance Imaging Demonstration of Anomalous Pulmonary Venous Drainage

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A "scimitar" shadow was found on routine chest roentgenography in an asymptomatic patient. Evaluation with cine magnetic resonance imaging demonstrated an anomalous pulmonary vein draining into the inferior vena cava below the diaphragm. The diagnosis of scimitar syndrome was confirmed and successfully repaired at operation. Cine magnetic resonance imaging may be of considerable value in the assessment of congenital pulmonary venous abnormalities and may provide an alternative to more traditional invasive diagnostic techniques in certain circumstances.

(Ann Thorac Surg 1990;50:121–3)

The scimitar syndrome is a rare and complex congenital anomaly, the essential feature of which is partial anomalous pulmonary venous connection (PAPVC) of part or all of the right lung to the inferior vena cava (IVC). The PAPVC causes a curvilinear shadow adjacent to the right heart border on chest roentgenography, giving the syndrome its memorable name [1]. Additional forms of cardiovascular abnormalities have been described in approximately 25% of individuals. The most common is an atrial septal defect (ASD). A variety of extracardiac abnormalities are frequently associated with the scimitar syndrome.

Although chest roentgenography often suggests the diagnosis, a variety of imaging techniques have been used to better define the anatomy. We present a case in which the presence of a scimitar vein was confirmed by cine magnetic resonance imaging (MRI).

A 26-year-old asymptomatic man was noted to have a cardiac murmur on preemployment physical examination. There was no history of previous cardiac conditions or symptoms. The physical examination was normal, except for a grade 1/4 systolic ejection murmur at the pulmonary area. The chest roentgenogram was consistent with increased pulmonary flow. A curvilinear density paralleling the right cardiac border suggested a scimitar vein of PAPVC (Fig 1). The two-dimensional echocardiogram demonstrated right ventricular enlargement with abnormal septal motion compatible with right ventricular volume overload. The remaining chambers were of normal size and contractility. The valves appeared normal. A Doppler echocardiographic study indicated a left-to-right shunt. A microbubble study also suggested an ASD. The electrocardiogram demonstrated right-axis deviation and first degree heart block. A technetium pertechnetate first-pass nuclear study demonstrated a left-to-right shunt of 2.3 to 1.

Cardiac catheterization confirmed the presence of a large anomalous right pulmonary vein that entered the IVC below the diaphragm. The oxygen saturation at this level was 98%. The mean right and left atrial pressures were equal at 7 mm Hg. An oxygen saturation curve confirmed left-to-right pulmonary to systemic shunt ratio of 1.9 to 1. Pulmonary arteriography showed PAPVC on the right and a secundum-type ASD.

A thoracoabdominal aortogram was normal. Standard magnetic resonance imaging was performed. The scimitar vein could be identified but with some difficulty as there was little contrast with the adjacent low-signal-intensity lung (Fig 2).

The PAPVC and its relationship to the IVC was then evaluated with a cine MRI technique. With this technique, the scimitar vein was well visualized, demonstrating excellent contrast with the adjacent lung (Fig 3). The real-time dynamics of the cine MRI were similar to that of the venous phase of pulmonary angiography.

The patient underwent open repair of the anomalous right pulmonary venous drainage and closure of a secundum ASD on cardiopulmonary bypass. The ASD measured 1.5 by 1.8 cm in diameter. The anomalous scimitar vein measured 1.5 by 2 cm in diameter and paralleled the right heart border in an intrapleural position. The vein joined the IVC just below the diaphragm at the level of the confluence of the hepatic veins. The anomalous right pulmonary vein was ligated at the level of the IVC, the pericardium posterior to the phrenic nerve was opened, and a side-to-side anastomosis of the vein with the left

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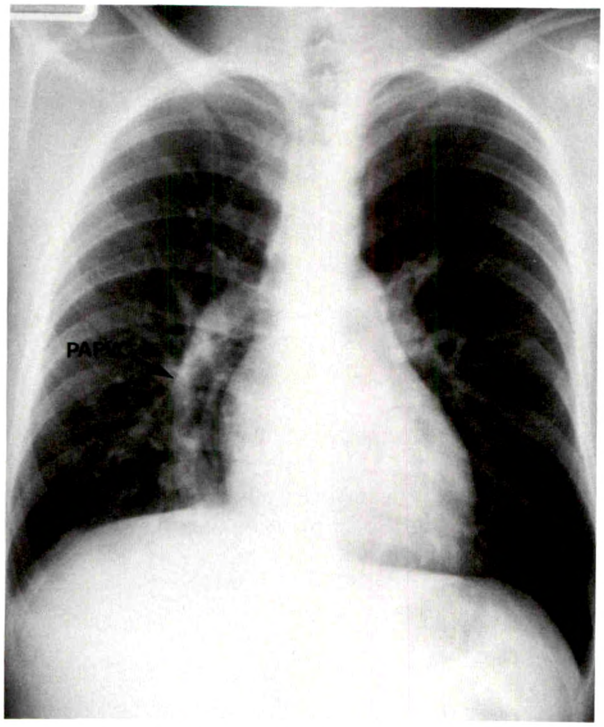

Fig 1. Routine chest roentgenogram demonstrating "scimitar" partial anomalous pulmonary venous connection (PAPVC) coursing to the inferior vena cava at the level of the diaphragm.

atrium was performed. The ASD was closed through the right atrium.

The patient had an uneventful recovery and was discharged from the hospital in stable condition on the eighth postoperative day.

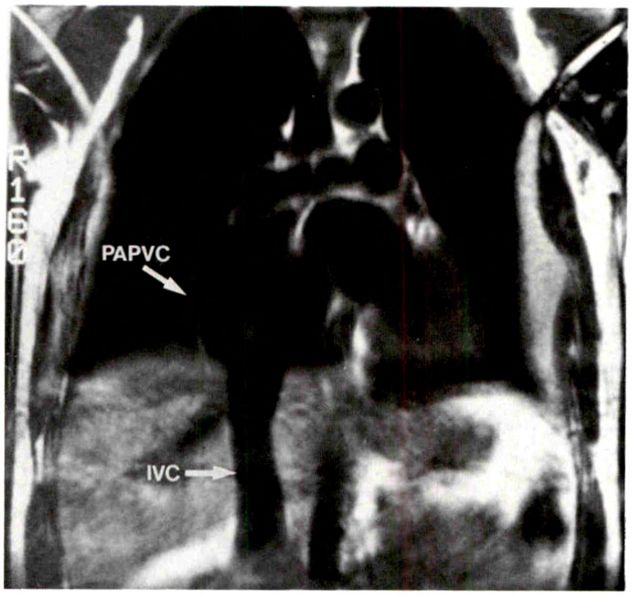

Fig 2. Spin-echo magnetic resonance image (coronal section) with partial anomalous pulmonary venous connection (PAPVC) to the inferior vena cava (IVC). Note poor contrast resolution between PAPVC and adjacent lung.

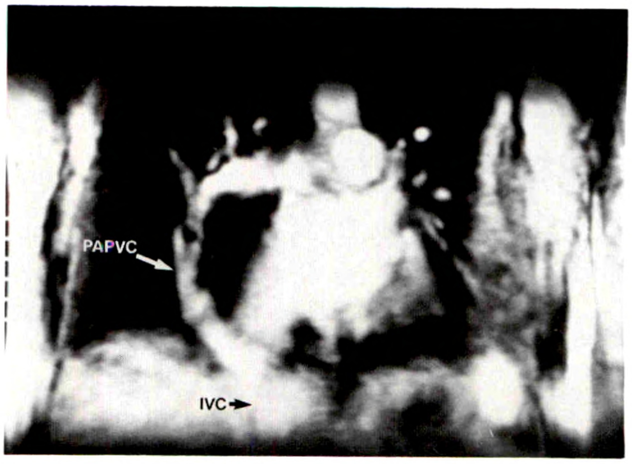

Fig 3. Cine magnetic resonance image (coronal section) demonstrating excellent contrast resolution between partial anomalous pulmonary venous connection (PAPVC) and adjacent lung. Infradiaphragmatic inferior vena cava (IVC) is also well demonstrated.

Comment

The first 2 cases of scimitar syndrome were reported in 1836 [2, 3]. Since that time, approximately 150 cases have been reported. Most cases of scimitar syndrome are identified by characteristic findings on routine chest roentgenography [4].

Although the chest roentgenogram may appear pathognomonic of scimitar syndrome, further imaging is necessary to confirm the diagnosis. In addition, further imaging can reveal associated anomalies, which may be important if surgical correction is contemplated. Arteriography is considered to be the most helpful study. Intravenous digital subtraction angiography [5], two-dimensional ultrasonography [6], and computed tomographic scans [7] have also been employed to evaluate PAPVC anatomy.

Magnetic resonance imaging is the most recent advance in cross-sectional imaging. One reported case of scimitar syndrome has been evaluated by standard MRI methods [8]. Conventional spin-echo MRI images show little or no signal in blood vessels, particularly when there is rapidly flowing blood within the vessels. Consequently, there is difficulty visualizing blood vessels adjacent to lung, which itself returns little signal.

Recent cine MRI imaging techniques using low-flip angles, gradient-refocused echoes, and short repetition times have provided dynamic visualization of moving blood simultaneously with high-resolution images. Cine MRI results in high-resolution anatomic images of cardiac chambers and major blood vessels that simulated angiography. The method is entirely noninvasive, and there is no exposure to ionizing radiation or intravenous contrast medium.

In our patient, we were able to visualize the scimitar PAPVC and to determine its important relationship with the IVC and the diaphragm. The cine images of the anomalous vein were as good as that of the venous phase pulmonary arteriography.

In summary, limitations exist in imaging mobile intracardiac structures with current MRI technology. However, the cine MRI technique provides excellent visualization of pulmonary vascular anatomy. Although arteriography remains the standard for evaluation of complex congenital cardiac defects, the use of cine MRI and other noninvasive modalities may obviate the need for more expensive and invasive procedures in selected patients.

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Disruption of a Modified Blalock-Taussig Shunt by Rapid Deceleration Injury

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A case is presented of an 8-year-old child who had tension hemothorax after disruption of a modified Blalock-Taussig shunt 2 weeks postoperatively. A rapid deceleration mechanism was responsible for the injury.

(Ann Thorac Surg 1990;50:124)

Complications associated with modified Blalock-Taussig shunting procedures are unusual [1, 2]. These complications primarily consist of early and late graft closure and development of pulmonary vascular disease [3, 4]. We report a case of traumatic disruption of the pulmonary artery and subclavian anastomosis.

An 8-year-old boy underwent a 6-mm Gore-Tex (W. L. Gore & Assoc, Flagstaff, AZ) left modified Blalock-Taussig shunt for severe tetralogy of Fallot with pulmonary atresia. He convalesced satisfactorily and was dismissed on postoperative day 6. The family was given the usual instructions for limitations of physical activities such as bicycle riding, swimming, or rough playing for 6 weeks.

However, 1 week after dismissal the child was playing on a merry-go-round, which was being rapidly turned by his playmates. He was thrown from the merry-go-round at a high speed and landed on the ground bruising his right knee and thigh. No apparent serious injuries were noted at that time. Soon after the event, the patient began to complain of general malaise and weakness. On returning home, he collapsed and was taken to the emergency department, where he became markedly unstable hemodynamically. The patient exhibited a marked decrease in systolic blood pressure and respiratory function. The chest roentgenogram showed a large fluid collection in the left side of the chest. A small-bore chest tube was placed and 80 mL of bright red blood was obtained. The patient's hemodynamic status continued to deteriorate, and he was transferred by helicopter to our institution for surgical evaluation with a diagnosis of left hemothorax. On admission, the patient's hemodynamic status had deteriorated further and he was in shock. No shunt murmur or breath sounds were audible in the left side of the thorax. Adequate venous access was obtained and fluid resuscitation was begun. A large-bore intrathoracic catheter was placed on the left side of the thorax and 800 mL of bright red blood was obtained. The patient's systolic blood pressure rose from 30 mm Hg to 120 mm Hg immediately on evacuation of the left side of the chest.

The patient was taken to the operating room and the left side of the chest was explored. The Blalock-Taussig shunt anastomoses exhibited two areas of dehiscence: one at the distal anastomosis and one at the proximal anastomosis. The shunt was of adequate length and was widely patent. The tears in the pulmonary and subclavian arteries were repaired, and the patient was transferred in satisfactory condition to the intensive care unit. The patient made an uneventful recovery.

Comment

Acceleration and deceleration injuries are well-known mechanisms for tearing of vascular structures [5]. Recent reports have also demonstrated that this mechanism of injury is associated with pacemaker lead fracture [6]. This case demonstrates that prosthetic vascular grafts may also be disrupted by this mechanism. Our patient sustained an acceleration/deceleration injury secondary to being thrown from a merry-go-round at a high speed. We believe that this caused a tension to be applied to the 2-week-old Blalock-Taussig shunt resulting in disruption of the distal and proximal anastomoses even though the shunt was of adequate length. This produced a life-threatening situation that only timely intervention prevented from being fatal.

This case underscores the need for a strict adherence by patients to limitation of physical activity after surgical procedures of this type. It also illustrates an unusual mechanism for disruption of a vascular prosthesis.

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Internal Mammary Artery Bypass After the Arterial Switch Operation

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Myocardial ischemia may ensue after coronary artery translocation during the arterial switch operation. We report the successful use of a right internal mammary artery to right coronary artery bypass graft in an infant with angiographic documentation of persistent graft patency 6 months postoperatively.

(Ann Thorac Surg 1990;50:125–6)

Since its initial description by Jatene and colleagues [1] in 1976, the arterial switch operation has become an accepted surgical treatment of infants with d-transposition of the great arteries. Successful translocation of the coronary arteries is the key to survival [2]. Coronary artery abnormalities, present in as many as one third of patients, usually do not preclude a successful outcome, as reported by a recent multicenter study [3]. Technical difficulties, however, have been encountered in infants with intramural passage of the left coronary artery and with subsequent impaired myocardial perfusion [3–5].

We report the successful use of a right internal mammary artery to right coronary artery anastomosis during the arterial switch operation in a neonate with d-transposition of the great arteries, a ventricular septal defect, and an abnormal right coronary artery.

A 3.2-kg male infant was referred for evaluation of cyanosis on the first day of life. The infant's physical examination, chest roentgenogram, and electrocardiogram were consistent with the echocardiographic findings of d-transposition of the great arteries, a 7-mm perimembranous ventricular septal defect, and a patent ductus arteriosus. He underwent cardiac catheterization and balloon atrial septostomy shortly after admission. The aortic root injection showed normal coronary artery distribution.

On day 9, the infant underwent the arterial switch operation with closure of the large perimembranous ventricular septal defect and the atrial septal defect and ligation of the patent ductus arteriosus. There was an oblique relationship between the aorta and the pulmonary artery. The aorta was transected just above the sinuses of Valsalva; the pulmonary artery was transected above its sinuses and was reanastomosed using the LeCompte maneuver. Inspection of the coronary artery anatomy showed the left coronary artery to originate normally from the left-facing sinus of Valsalva (according to the nomenclature of Gittenberger-de Groot [4]), and the right coronary artery to originate from the posterior-facing sinus of Valsalva.

The right coronary artery was noted to course briefly within the aortic wall, exiting closer to the interostial commissure than normal. The left coronary artery was excised with a button of aortic tissue; however, when the right coronary artery was excised, little aortic tissue was available for anastomosis with the neoaorta, although the anastomosis was completed using 7-0 Prolene suture (Ethicon, Somerville, NJ). On rewarming, the inferior wall of the heart became cyanotic; hence, the right internal mammary artery was dissected free from the chest wall and anastomosed end-to-side to the right coronary artery. Myocardial perfusion improved dramatically, and the infant was readily weaned from cardiopulmonary bypass. He was discharged on the 13th postoperative day. The electrocardiogram showed complete right bundle-branch block with normal sinus rhythm at the time of discharge.

At 5 months of age and a weight of 6.5 kg, the infant underwent postoperative cardiac catheterization. There was no residual shunt by oximetry, and the right ventricular pressure was 42/5 mm Hg with a 25-mm Hg gradient across the supravalvar pulmonary region at the site of the anastomosis. By angiography in both the aortic root and the right innominate artery, there was normal left coronary artery flow and widely patent anastomosis between the right internal mammary artery and the right coronary artery (Fig 1). There was no anterograde flow through the proximal right coronary artery from the aortic root.

Comment

The use of an internal mammary to coronary artery graft is an acceptable option for patients with myocardial ischemia after coronary artery translocation during the arterial switch operation. Although this complication is relatively uncommon, it is a major cause of operative morbidity and mortality [2]. Anomalous coronary artery anatomy is not uncommon in d-transposition of the great arteries, although the arterial switch operation may be safely performed in most cases [3]. Intramural passage of a coronary artery is a major risk factor in coronary artery translocation, as excision of such a vessel may not allow removal of a sufficient-sized button of aortic tissue surrounding the coronary orifice to ensure patency of the coronary artery after translocation to the neoaorta.

Ebels and colleagues [6] reported the successful use of a

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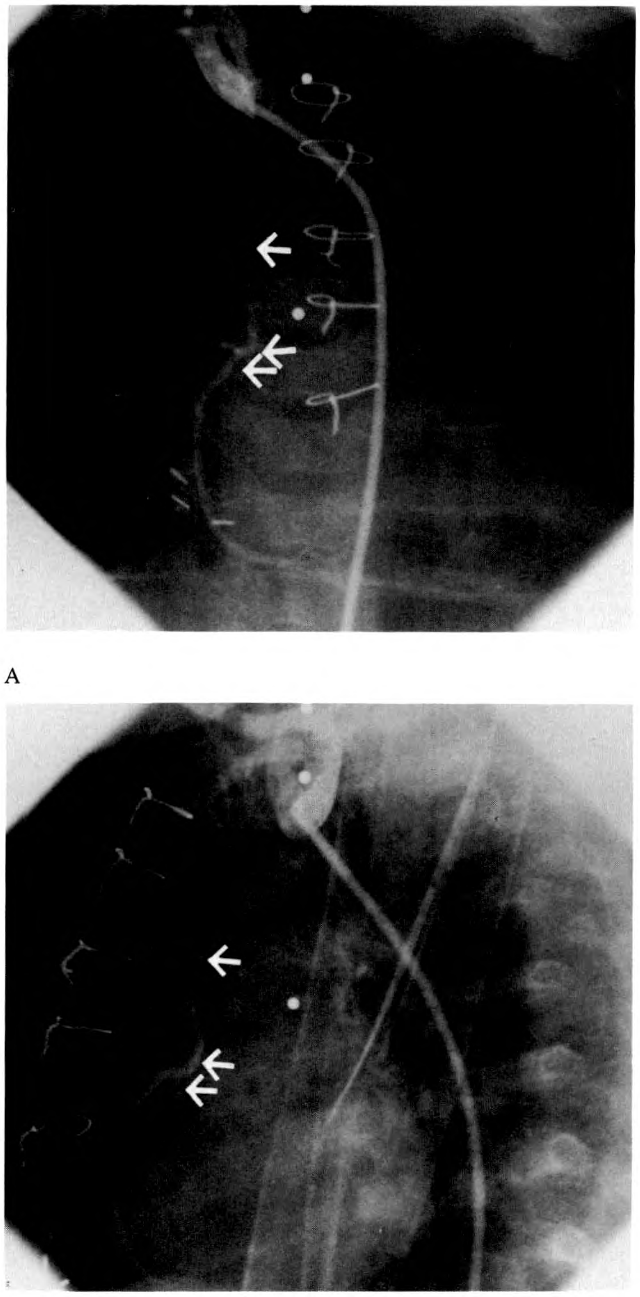

Fig 1. Injection into the right innominate artery shows prompt opacification of the right internal mammary artery (single arrow) *and its anastomosis to the right coronary artery* (double arrow) *in both the (A) anteroposterior and (B) left anterior oblique projections.*

left internal mammary artery to left coronary artery graft when myocardial ischemia ensued after the arterial switch operation in an infant with an intramural left coronary artery. In their patient, postoperative angiography during the neonatal period confirmed persistent patency of the graft. In our patient, persistent patency of the anastomosis 5 months later, along with excellent cardiac function both by angiography and by echocardiography, supports the use of the internal mammary artery to augment coronary perfusion during the arterial switch operation. We believe this technique is faster than and preferable to attempted revision of the coronary anastomosis for coronary insufficiency as multiple suture lines need not be taken down, the internal mammary artery is readily accessible, and the internal mammary artery is usually closely matched in size to the coronary artery.

Although the long-term fate of the right internal mammary to right coronary artery graft is unknown, we anticipate further growth of this vessel with growth of the patient. The technical expertise gleaned from advances in adult coronary artery surgery has helped facilitate this procedure and thereby allow for improved coronary perfusion and myocardial function when traditional coronary artery translocation is not possible or has failed during the arterial switch operation.

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Right Pneumonectomy Syndrome in Infancy Treated With an Expandable Prosthesis

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Severe respiratory distress developed in a 5-month-old infant approximately ten days after pneumonectomy for complete sequestration of the right lung. Right pneumonectomy syndrome was diagnosed by bronchography, which revealed thinning and obstruction of the left main bronchus during expiration. A right thoracotomy was then performed, and an inflatable tissue expander with a subcutaneous injection port was inserted into the right chest cavity to prevent recurrence of the mediastinal shift and to allow for future growth. The patient has done well, requiring reinjection of the prosthesis with additional volume on one occasion in a 20-month period of follow-up.

(Ann Thorac Surg 1990;50:127–9)

Severe mediastinal shift after right pneumonectomy has been described in children aged 2 months to 17 years [1–4]. This displacement of the heart, the great vessels, and the trachea can lead to bronchial stretching and vascular compression resulting in severe respiratory failure. Various intrapleural prostheses have been recommended to correct the mediastinal shift and relieve the bronchial obstruction in adults and older children [1, 3, 5]. Previous prostheses, however, were not expandable and theoretically would have to be repeatedly replaced if used in an infant. We have examined a 5-month-old infant with bronchial obstruction after right pneumonectomy who was treated by an intrapleural inflatable tissue expander to allow for future growth.

A 5-month-old, 6.1-kg female infant had recurrent pneumonia when admitted to our hospital. She was in mild respiratory distress with intercostal and suprasternal retractions without cyanosis. Breath sounds were decreased over the entire right lung, and occasional wheezes were detected on the left. Cardiac examination was normal. Chest roentgenogram showed haziness of right lung and hyperinflation of left lung. Cardiac size and configuration were normal. Right heart catheterization showed complete sequestration and hypoplasia of the right lung with a severely hypoplastic right pulmonary artery. Principal arterial supply of the right lung originated from the descending aorta below the diaphragm. Right pneumonectomy was performed, which was tolerated very well until approximately 10 days postoperatively, when rapidly progressive respiratory distress developed that required reintubation. Chest roentgenograms showed mild tracheal deviation with the heart and great vessels shifted into the right hemithorax. The child was rapidly weaned from ventilatory support and appeared to respond to bronchodilator therapy. Over the next several weeks, however, progressive shift of heart and mediastinal structures occurred, and increasingly frequent episodes of severe dyspnea, cyanosis, and bradycardia developed. Chest roentgenogram at this time showed marked tracheal deviation, and the heart was shifted against the right chest wall (Fig 1).

To prevent occlusion of the endotracheal tube by the deviated tracheal wall, the bevel had to be directed toward the left main bronchus. Flexible bronchoscopy was performed to investigate suspected intermittent bronchial obstruction. Because of the mediastinal shift, there was acute angulation of the left main bronchus–tracheal junction that precluded visualization of the bronchus. Bronchography showed the left main bronchus to be narrow and to obstruct during expiration (Fig 2). The trachea did not appear compromised nor was the obstruction pulsatile. Because vascular compression of the left main bronchus and trachea has been reported as a major cause of respiratory compromise in children after pneumonectomy [3, 4], cardiac catheterization was performed, which confirmed that the compression was not vascular.

Because of increasing difficulty in ventilating the patient, a right thoracotomy was performed. Adhesions were lysed between the costal and the diaphragmatic and mediastinal pleura, and the pericardium and mediastinal structures were dissected from the right chest wall. The pressure required to inflate the left lung decreased dramatically from 40 cm H_2O to 24 cm H_2O and the arterial carbon dioxide tension decreased from 58 to 36 mm Hg, although there was no change in minute ventilation. A 125-mL inflatable tissue expander (Surgitek) with a subcutaneous injection port was then inserted into the right pleural space and inflated with 60 mL of sterile saline solution. The prosthesis filled the right chest cavity and caused no hemodynamic changes. An additional 20 mL of fluid decreased systolic blood pressure by 10%, so this

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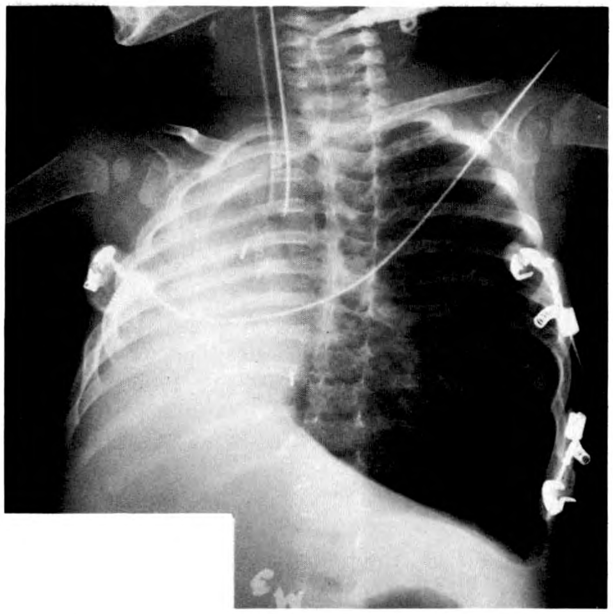


Fig 1. Preoperative chest roentgenogram showing marked tracheal deviation and hyperinflation of left lung.

20 mL of saline solution was withdrawn and the chest was closed. Postoperative chest roentgenograms showed the heart and mediastinal structures nearly returned to their natural position (Fig 3).

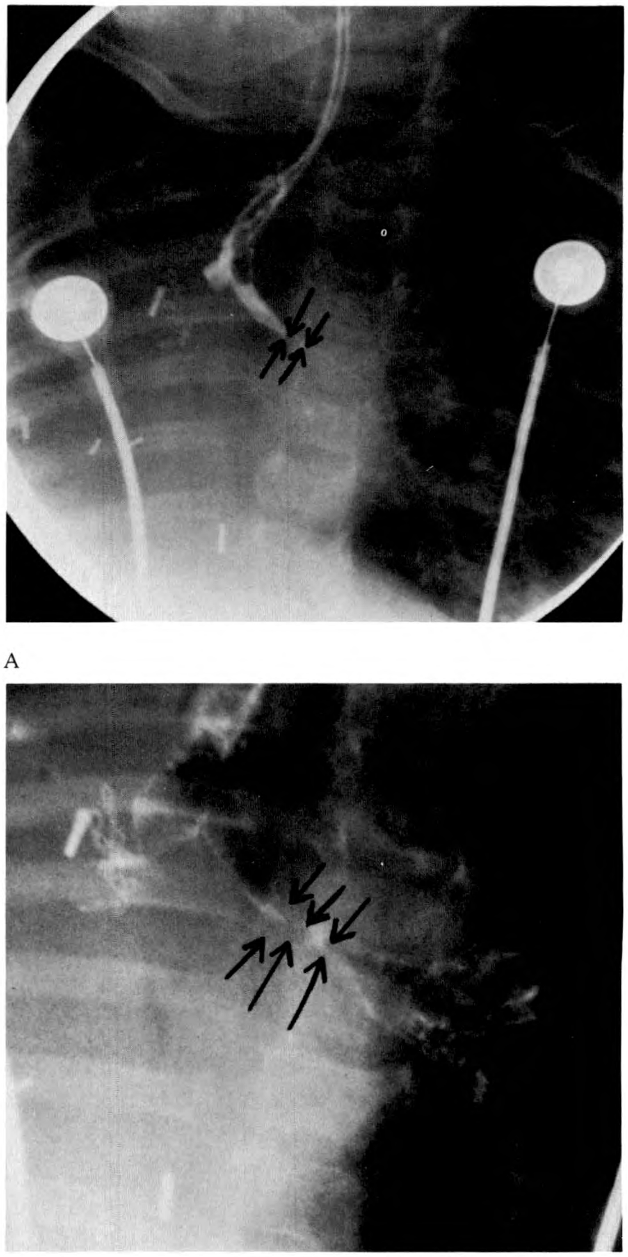
The infant was extubated without difficulty within 24 hours. She continued to have noisy respirations due to malacia of the left main bronchus, but she exhibited remarkable catch up growth (weight gain of 3.2 kg in the first 6 months after operation) and development. Five months after operation, increased wheezing developed in the infant, and she had mild mediastinal shift on chest roentgenography. Thirty milliliters of sterile saline solution injected into the prosthesis corrected both problems. Eight months after operation, the prosthesis developed a leak and was replaced without complication. For a follow-up period of 20 months the infant has done well, with progressive improvement in the bronchial malacia.

Comment

Mediastinal shift with symptoms of tracheal compression (right pneumonectomy syndrome) is a rare complication of pneumonectomy in both adults and children. These symptoms are more likely to develop in infants and young children presumably because of increased mobility of the mediastinum, increased elasticity and compliance of the remaining lung that allows overdistention, and greater compressibility of the trachea and bronchi, which have less cartilaginous support [1, 3]. Diagnosis may be difficult because of the intermittent and often sudden respiratory distress that can mimic gastroesophageal reflux, reactive airway disease, vascular ring, esophageal motility problems, or recurrent aspiration.

Prevention or treatment of the mediastinal shift with various types of intrapleural prostheses has been described, but most of these were employed in older infants, children, or adults. Devices such as Lucite balls, Silastic breast implants, and testicular prostheses have been used with success [1, 2, 6]. It is important, however, to make the distinction between pneumonectomy and lobectomy because the infant's lung will grow to fill the lobectomy space, and this process is indeed desirable. Insertion of a prosthesis in a lobectomy patient would be unnecessary as major shift of mediastinal structures does not occur and the prosthesis could retard growth of the ipsilateral lung.

Insertion of a Dacron graft between the ascending and



A

B

Fig 2. (A) Compression of left main bronchus (arrows) *during expiration with complete obstruction of lumen. (B) Thinning of left main bronchus* (arrows) *but improved lumen size during inspiration.*

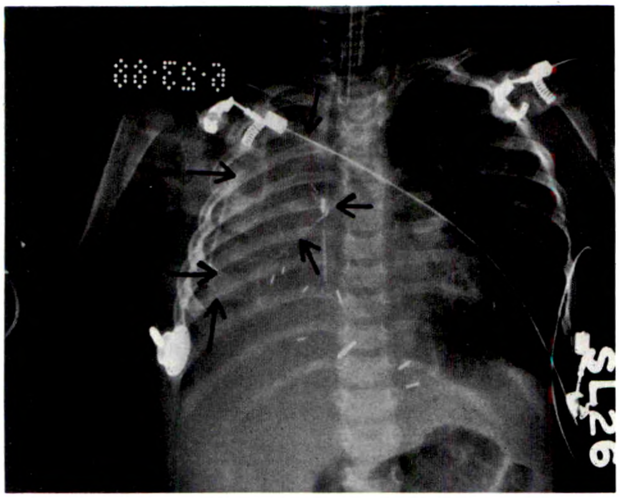


Fig 3. Postoperative chest roentgenogram showing prosthesis (arrows) *to prevent shift of mediastinal structures and improved air exchange to left lung with less hyperinflation.*

descending aorta with division of the aortic arch between the left carotid and subclavian arteries has also been described to treat vascular compression of the left main bronchus from mediastinal shift and displacement of heart and great vessels [4]. Suspension of the great vessels from the trachea and left main bronchus by suturing them to the posterior surface of the sternum has been attempted without success [7].

We elected to treat this problem with an intrapleural prosthesis as it appeared to be the lowest risk procedure with proven efficiency. Infants under 1 year of age with right pneumonectomy syndrome present a particular challenge, however, as they usually grow rapidly after a successful operation. The ideal prosthesis should therefore be expandable. For this reason, we selected a 125-mL Silastic tissue expander with subcutaneous injection port that would allow for increases in volume without general anesthesia or operation. Five months postoperatively, symptoms of increased respiratory distress developed in the infant owing to recurrence of mediastinal shift, which was alleviated by injection of 30 mL into the prosthesis, thus saving her an operation. Unfortunately, the device developed a leak 8 months postoperatively, requiring a second thoracotomy.

In summary, right pneumonectomy syndrome is a rare complication of complete lung resection in children, with infants being at highest risk. Diagnosis depends on a high index of suspicion as the syndrome may mimic a number of other respiratory and gastrointestinal problems. Use of an expandable pleural prosthesis appears to correct overshifting of the mediastinum and offers an advantage over a prosthesis with a fixed volume in the very young patient who will undergo a rapid growth phase.

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Isolated Left Carotid Artery in CHARGE Association: Diagnosis and Repair

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Isolation of the left carotid artery is extremely rare. We report a case of isolation of the left carotid artery with CHARGE association. Aortic arch abnormalities should be looked for in all children with CHARGE association. The technique of repair involved implantation of the isolated left carotid artery to the ascending aorta.

(Ann Thorac Surg 1990;50:130–2)

Based on Edwards' double-arch theory, variations of aortic arch branching are the result of interruption of the primitive double arch at an abnormal position [1, 2]. Rare cases of isolation could presumably be the result of "double breaks," such as that yielding an isolated left subclavian artery or left innominate artery [3, 4]. In our review of the literature, there has been a single report of a patient with an isolated left common carotid artery that arose from the left pulmonary artery [4]. This dysmorphic child had physiologic "steal" from the cerebral circulation that was surgically repaired through a left thoracotomy with ligation of the left common carotid artery at its origin.

We encountered an infant with CHARGE association, a complex that includes *c*oloboma, *h*eart disease, choanal *a*tresia, growth and mental *r*etardation, *g*enital hypoplasia, and *e*ar anomalies [5]. In addition, the infant had a right aortic arch with an isolated left common carotid artery arising from the main pulmonary artery and thymic hypoplasia. She successfully underwent carotid implantation to the ascending aorta yielding complete anatomical correction of the vascular malformation.

A 3.2-kg baby girl was delivered at term to a 26-year-old primiparous woman. Examination at birth disclosed dysmorphic pinnae, hypoplasia of left side of the face, left facial weakness, normal genitalia, and short eyelashes. Results of ophthalmoscopic examination were negative. Chest roentgenogram demonstrated a right aortic arch, levocardia with situs solitus, 11 ribs bilaterally, and mild pulmonary over-circulation. A holosystolic murmur was present. Two-dimensional and Doppler echocardiography demonstrated a patent ductus arteriosus with a large atrial septal defect secundum. An axial computed tomographic scan of the head showed a normal brain with right choanal atresia. Because of feeding difficulties with poor suck, apnea, and episodes of cyanosis, the child underwent ligation of a right-sided patent ductus arteriosus transpericardially through a left thoracotomy at 6 days of age. Intraoperatively, a vessel arising from the main pulmonary artery and coursing into the neck consistent with an isolated left carotid artery was noted. The idea of ligation was entertained, but it was not performed as further diagnostic confirmation was needed. The infant continued to have intermittent cyanotic episodes associated with poor feeding. Postoperative two-dimensional and Doppler echocardiograms demonstrated the left carotid artery arising from the main pulmonary artery with moderate shunting and aortic flow reversal.

When the infant was 23 days of age, cardiac catheterization was performed. A left-to-right shunt was observed at the atrial level with a pulmonary/systemic blood flow ratio of 3.4 and a pulmonary arterial pressure of 40/15 mm Hg. Left ventriculography showed retrograde filling of the left common carotid artery and opacification of the main pulmonary artery and branches. The first branch off the ascending aorta was the right subclavian artery, followed by the right common carotid artery and an aberrant left subclavian artery arising from a retroesophageal aortic diverticulum (Fig 1). Selective injection of the right common carotid artery with digital subtraction showed retrograde filling of the left carotid system (Fig 2). Collateral flow from the posterior circulation was not present on right vertebral artery injection. A single photon emission computed tomographic brain scan showed segmentally decreased perfusion of the left cerebral cortex. When the infant was 6½ weeks of age, the isolated left common carotid artery was implanted onto the ascending aorta through a median sternotomy with partial crossclamping of the aorta (Fig 3). A 4-mm punch was used for the aortotomy, and a 7.0 polydioxanone suture was used for the anastomosis [6]. There was severe hypoplasia of the thymus consisting of a 1-cm-diameter mass of tissue with absence of the right and left lobes. A biopsy revealed histologically unremarkable thymic tissue. The postoperative course was uneventful without any recurrences of the episodes of apnea or cyanosis. A follow-up 1 year postoperatively revealed normal antegrade flow in the left carotid artery by two-dimensional and Doppler echocardiography and magnetic resonance imaging flow studies.

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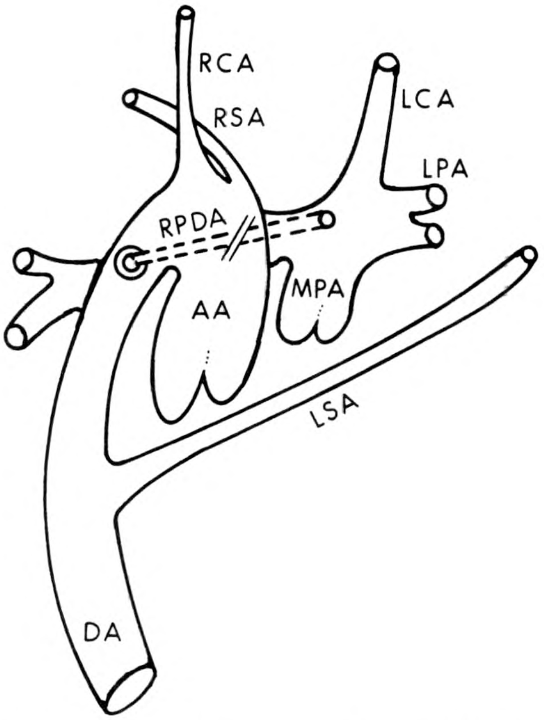

Fig 1. The aortic arch anomalies. (AA = *right aortic arch;* DA = *descending aorta;* LCA = *isolated left carotid artery;* LPA = *left pulmonary artery;* LSA = *aberrant left subclavian artery;* MPA = *main pulmonary artery;* RCA = *right carotid artery;* RPDA = *right patent ductus arteriosus;* RSA = *right subclavian artery.)*

Comment

Right aortic arch with a congenital vascular anomaly resulting in the steal phenomenon is rare, and only a handful of cases have been reported. This report describes the second case of a right aortic arch with an isolated left common carotid artery from the pulmonary artery. Based on Edwards' double-arch theory, Fong and Venables [4] postulated that the distal migration of the left subclavian artery beyond the ductus arteriosus leads to a left ductus that enters the left dorsal aortic root just proximal to the origin of the left subclavian artery. With subsequent disappearance of segments B and D of the left aortic arch, an isolated left common carotid artery and an aberrant left subclavian artery are produced [4]. Alternatively, if one does not use the Edwards hypothesis, one would have to postulate that the left common carotid artery arose directly from the pulmonary artery without an interposing segment of ductus arteriosus.

In a review of the types of congenital heart disease found in 53 patients with CHARGE association, Lin and colleagues [7] reported that 42% (22/53) had a conotruncal abnormality. Ninety-one percent (20/22) of the conotruncal abnormalities were tetralogy of Fallot or double-outlet right ventricle. Thirty-six percent of patients (19/53) had an aortic arch anomaly, of which 72% (13/19) had an aberrant subclavian artery. Aortic arch abnormalities are common in CHARGE association, and this case demonstrates that isolation of the left carotid artery should be included in the spectrum of symptomatic anomalies.

Diagnosis of such vascular anomalies may not be apparent initially, but they should be considered in infants with CHARGE association. Physical examination, chest roentgenography, barium swallow, and echocardiography may alert the physician to the presence of symptomatic variations of the great vessels at birth. However, the definitive diagnosis can only be made with aortography and selective arteriography of the great vessels. Late retrograde filling of the left common carotid artery and opacification of the pulmonary artery are diagnostic of an aberrant left common carotid artery arising from the pulmonary artery.

We have described a new surgical technique for anatomical correction of left-to-right shunting and the subsequent steal from the cerebral circulation. Previously reported surgical repair was simple ligation of the left common carotid artery at its origin based on the assumption that the cerebral circulation would be adequately perfused through the right common carotid artery and the posterior circulation. In our patient, a single photon emission computed tomographic brain scan showed hypoperfusion thought to be leading to ischemia of the left brain, and subsequent ligation of the left common carotid artery was believed to be hazardous. Therefore, through a median sternotomy, the carotid artery was implanted

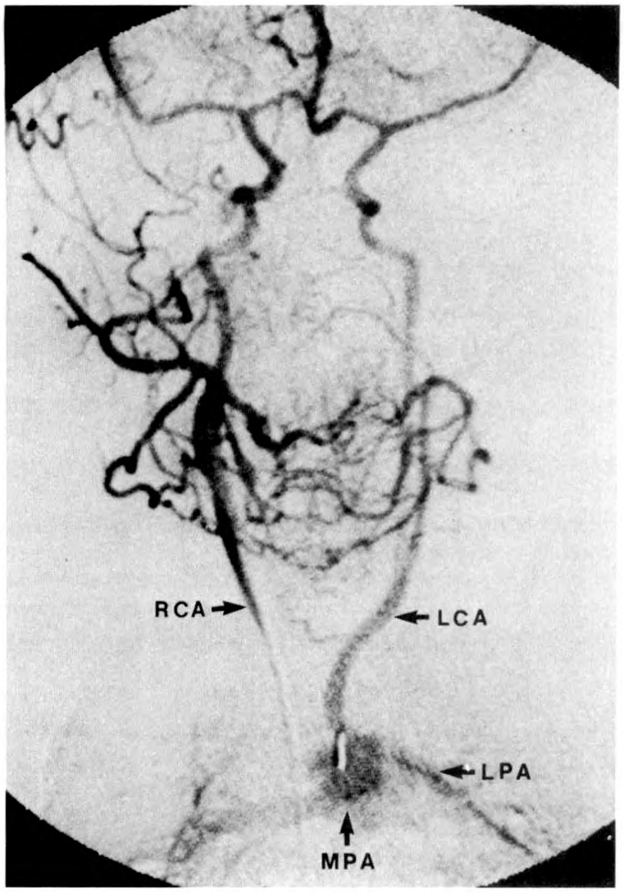

Fig 2. Digital subtraction angiogram of the right carotid artery injection. (LCA = *isolated left carotid artery;* LPA = *left pulmonary artery;* MPA = *main pulmonary artery;* RCA = *right carotid artery.)*

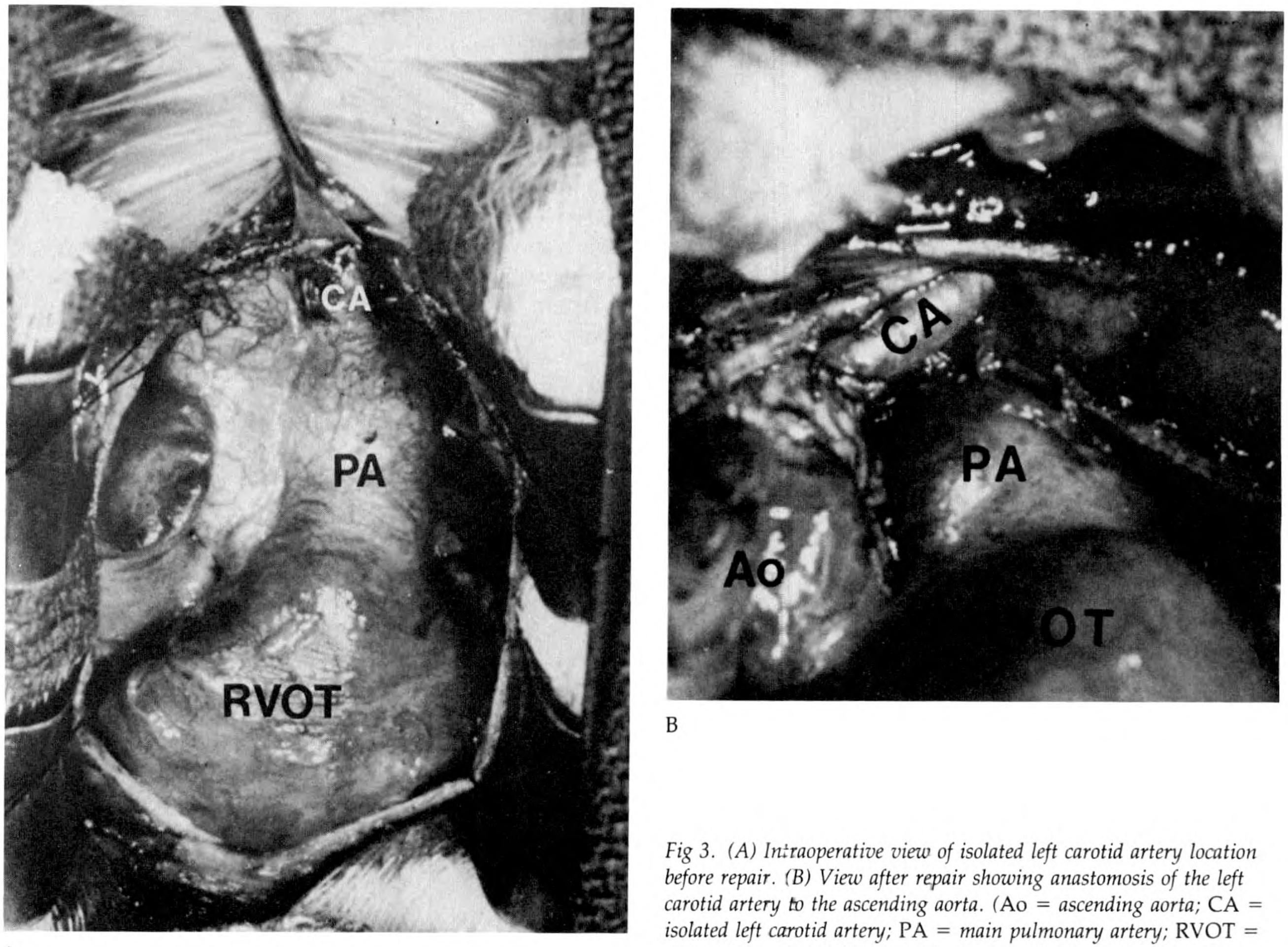

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Fig 3. *(A) Intraoperative view of isolated left carotid artery location before repair. (B) View after repair showing anastomosis of the left carotid artery to the ascending aorta.* (Ao = *ascending aorta;* CA = *isolated left carotid artery;* PA = *main pulmonary artery;* RVOT = *right ventricular outflow tract.)*

onto the aortic arch to achieve a superior physiological result.

Our experience supports anatomical correction with aortic implantation of the isolated great vessel as the procedure of choice in symptomatic infants with isolation of a great vessel creating a steal phenomenon.

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Retrotracheal Goiter: A Diagnostic and Therapeutic Problem

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A patient with chronic cough and recent dysphagia was found to have a retrotracheal mass extending into the visceral mediastinum on chest roentgenogram. A computed tomographic scan confirmed a retrotracheal lesion, which was believed to be of lymphatic origin. A thyroid scan demonstrated downward displacement of the left lobe but little uptake in the mass. Histological findings of mediastinal biopsies were inconclusive. A large retrotracheal thyroid adenoma was easily excised through a right thoracotomy. The approach to diagnosis and, in cases of doubt, the safety of surgical access through thoracotomy for thyroid lesions in this unusual site is discussed.

(Ann Thorac Surg 1990;50:133–5)

Thyroid masses extend into the thorax in approximately 6% of patients and up to 15% of these are malignant [1]. The majority are immediately retrosternal, and such patients usually are seen because of pressure symptoms. Goiters extending in the retrotracheal plane are uncommonly reported [2, 3] as 90% of masses in this region are neurogenic in origin, the remainder being mostly vascular. This report highlights the investigative difficulties associated with retrotracheal goiters and the importance of accurate diagnosis with regard to approach to treatment.

A 69-year-old male patient was observed to have a nonproductive cough associated with dyspnea on exertion and recent dysphagia for solid foods. Clinical examination revealed tracheal deviation to the right side. Chest roentgenogram demonstrated a soft tissue mass to the right of the midline in the upper visceral mediastinum pushing the trachea forward (Fig 1). Full blood count; thyroid and liver function tests; and levels of urea and electrolytes, serum calcium and phosphate, serum α-fetoprotein, β-human chorionic gonadotropin, and carcinoembryonic antigen were all normal. An arch aortogram was normal. A computed tomographic (CT) scan of the mediastinum showed that the mass extended above the sternal notch, behind and to the left of the trachea and downward in the retrotracheal region toward the subcarinal area. It appeared well defined and encapsulated, and the CT scan appearances were believed to favor a diagnosis of metastatic mediastinal lymphadenopathy (Fig 2). A radioiodide thyroid scan demonstrated displacement of the right lobe of thyroid to the right, whereas the lateral aspect of the left lobe was displaced downward with little uptake of isotope in the area of the mediastinal mass. Bronchoscopy showed a narrowed trachea compressed from behind. Multiple biopsy specimens taken at mediastinoscopy appeared benign with some evidence of capsular tissue.

As CT scans favored mediastinal lymphadenopathy and as radioisotope scintigraphy was not completely conclusive, a right thoracotomy was performed through the fourth intercostal space. A large well-encapsulated tumor extended from the left side between the trachea and esophagus, compressing both these structures. After ligation of the blood supply through the upper pedicle, the mass was completely excised without difficulty. Histological analysis showed a large microfollicular adenoma of the thyroid with marked degenerative changes, but no malignancy was noted.

Comment

Thyroid lesions extending into the retrotracheal plane are uncommon. Accurate preoperative diagnosis is important in the management of this condition. Appropriate diagnostic methods are discussed in recent publications [4, 5], which suggest that radioisotope scanning may be misleading and that CT scanning is often a more accurate tool in diagnosis. Homogenicity, calcification in the mass, and demonstration of a connection with the cervical thyroid are considered diagnostic features on CT scan. Neither of these investigations proved to be diagnostic in our patient, the CT appearances being in favor of mediastinal lymphadenopathy. However, on retrospective review of the CT scans in this case it seems that detailed assessment of the junctional zone between the mass and the cervical thyroid was not possible, the highest cut being just above the sternoclavicular joints (Fig 2).

The surgical approach to excision of intrathoracic goiters can vary. Most can be excised through a cervical incision. However, in the few reports on retrotracheal

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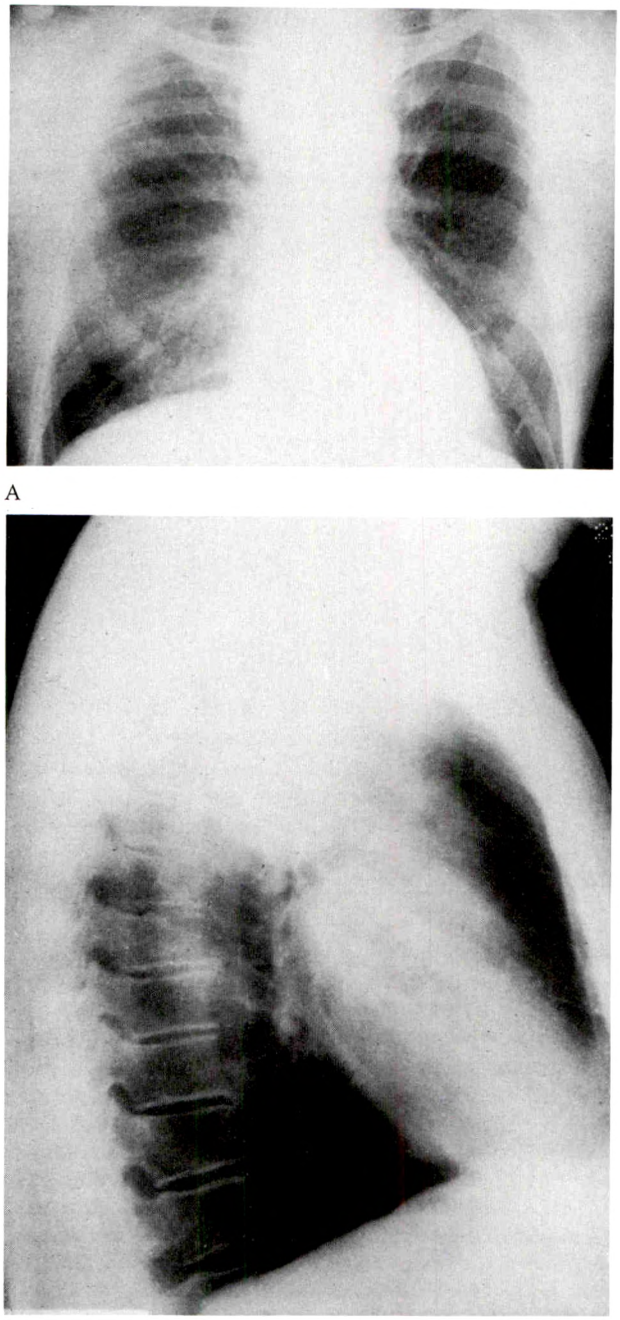

Fig 1. (A) Posteroanterior chest roentgenogram showing the mass in the upper visceral mediastinum to the right of the midline and which, on the lateral view (B), is displacing the trachea forward.

goiter [2, 3], a thoracotomy was performed on most patients to allow full access to the mass. Although the goiter in our report probably could have been removed through a cervical approach, the decision to use a thoracotomy was largely based on the inconclusive outcome of the preoperative investigations. A cervical incision would not be adequate to deal with an isolated thyroid lesion in the mediastinum, as such lesions usually derive their blood supply from an intrathoracic source. Both CT and radioisotope scans were unable to demonstrate a definite connection between the mass and the cervical thyroid in this patient. Isolated thyroid lesions have been described in the tracheal wall [6, 7], in the intracardiac area [8], and in the larynx, esophagus, aorta, and pericardium [9].

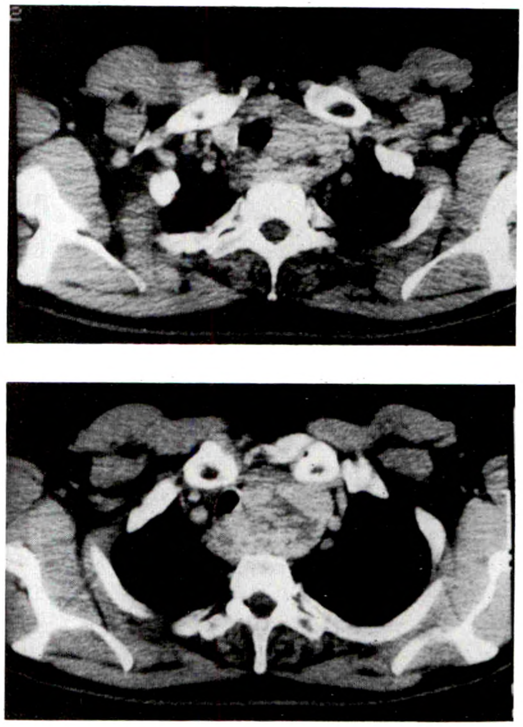

Fig 2. Computed tomographic scan demonstrating the lack of definition of a connection between the mediastinal mass and the cervical thyroid gland.

Precise diagnosis of the nature and site of the mass and the presence of communication with the cervical thyroid are therefore of great importance in the management of this condition. Our patient illustrates the problem in establishing these preoperative criteria and highlights the importance of accurately demonstrating the relationship of the mass to the thyroid gland using CT scanning in the investigation of retrotracheal masses. Although radioisotope scanning is known to be a useful test for delineating the presence of functioning thyroid tissue in the mediastinum, CT scanning can provide additional and often better anatomical information [10]. Thoracotomy or median sternotomy is probably the best surgical approach for cases in which diagnostic confusion exists. If the patient is comprehensively investigated to exclude neurological and vascular disorders and is being managed in a unit with expertise in this area of surgery, thoracotomy or median sternotomy should result in a satisfactory outcome. However, CT scanning should allow accurate diagnosis in the majority of patients.

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REVIEW OF RECENT BOOKS

Vascular Surgery, Third Edition

Edited by Robert B. Rutherford
Philadelphia, W.B. Saunders, 1989
1,912 pp, illustrated, $195.00

Reviewed by A. M. Graham, MD, FRCS(C)

The third edition of the textbook, *Vascular Surgery*, edited by Dr Rutherford, has undergone a major reorganization from previous editions, as well as having numerous additions. These changes parallel the expanding and exciting field of vascular surgery. The textbook offers an international flavor throughout its reading, in that the authors come from all corners of the world, which provides an expanded view of a number of problems that we deal with.

The organization of each section of the text has been markedly improved so that the reader is able to review one area quite nicely without having to scatter throughout the book. Each section editor has done a good job in leading the reader through the subject matter in an elegant manner.

The additions to the text include an expanded area in basic science with respect to atherosclerosis and its pathogenesis, as well as an expansion and reorganization of the common complications that are seen in vascular surgery. Up-to-date topics involving "state-of-the-art" investigative instrumentation are presented involving review of magnetic resonance imaging, laser Doppler, and vascular imaging techniques such as the duplex scan and positron emission tomography.

The major strength of this textbook is the fact that the authors are truly world experts in their fields. Examples of this are discussions of arterial autographs and endarterectomies by Dr Stoney, the chapter of in situ bypass grafts by Dr Leather, and of course the excellent review of the management of extracranial cerebrovascular disease by Dr Moore.

The editorial staff and the Section Chiefs in the textbook have been able to improve the consistency of the chapters within each section. The previous problem of inconsistent chapter authorship has been minimized, undoubtedly through very strict editorial review. However, within an extensive book such as this, a critical eye will find faults. One of these faults, I believe, lies in that certain areas are not covered very extensively and could easily be improved upon. One of these areas is with respect to the role of endarterectomy in aortorenal and aortoiliac occlusive disease. Although not performed frequently in many centers, it is still an important procedure for all vascular surgeons to be up to date on. Another area in that respect involves endovascular procedures. The role of laser probes, artherectomy devices, and intravascular stents has yet to be properly defined, but because of the intense interest in them at this time, further discussion in this textbook would be appropriate. The preface of the text justifies the limited coverage of this, but I feel an expanded chapter would be suitable.

In summary, this textbook is truly a delight to read and this new edition has strengthened its role as the premiere information source for both the vascular surgeon and the trainee. It is highly recommended as the multiple-author method has been refined within this edition.

Montreal, Canada

Severe Hemolysis After Incomplete Mitral Valve Repair

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We report 2 cases of severe intravascular hemolysis after mitral valve repair using a Duran annuloplasty ring. In both patients residual mitral regurgitation was present, hemolysis was severe enough to warrant a second operation, and hemolysis ceased immediately after the second operation. We believe that a high-velocity regurgitant jet directed toward the cloth-covered annuloplasty ring was responsible for the hemolysis in both patients.

(Ann Thorac Surg 1990;50:136–7)

Recent reports suggest that mitral valve repair may be associated with a lower long-term morbidity and mortality than mitral valve replacement [1]. As reparative operations become more common, unusual complications such as hemolysis will likely be reported more frequently. Intravascular hemolysis has been reported with a variety of postoperative lesions. Some degree of hemolysis can occur with normally functioning mechanical prostheses, the severity of which varies with the prosthetic design [2]. Severe hemolysis has been associated with paraprosthetic regurgitation and has occurred after attempts to repair these defects [3]. Hemolysis has been reported with damaged or calcified porcine prosthetic leaflets [4] and with bent valve struts [5]. It has also been reported after an attempt to repair torn mitral chordae [6]. We are aware of only one previous report of severe hemolysis after mitral valve repair using an annuloplasty ring, and in that case there was a dehiscence of the annuloplasty ring [7]. In our 2 patients, the annuloplasty ring was well seated at repeat operation.

Patient 1

A 71-year-old man with chronic mitral regurgitation due to myxomatous degeneration of the mitral valve underwent valve repair because of increasing symptoms of dyspnea on exertion and evidence of ruptured chordae tendineae on echocardiography. Preoperative angiography demonstrated 3+ to 4+ mitral regurgitation and a clinically significant lesion in the left anterior descending coronary artery. Exploration of the valve revealed ruptured chordae to the posterior leaflet. The valve was repaired by quadrangular resection of the posterior leaflet, repair of the torn chordae, and annuloplasty with a No. 33 Duran ring. The lesion in the left anterior descending coronary artery was bypassed with an internal mammary artery graft. Intraoperative Doppler echocardiography after the surgical repair showed a small regurgitant jet at the medial aspect of the repair.

Two months after operation, a severe anemia was detected. The hemoglobin level had fallen from 0.1 g/L (0.01 g/dL) at discharge to 0.076 g/L (0.0076 g/dL). His peripheral smear showed schistocytes; he had gross hemoglobinuria, the lactic dehydrogenase level was elevated, and the haptoglobin level was low. A diagnosis of intravascular hemolysis was made. Postoperative Doppler examination showed only mild mitral regurgitation with a medially directed regurgitant jet. Repeat catheterization showed 2+ mitral regurgitation. Because of unremitting hemolysis requiring multiple transfusions, he underwent replacement of the mitral valve with a Medtronic-Hall prosthesis.

Inspection of the annuloplasty ring at operation showed no evidence of dehiscence, but the area of the annuloplasty ring adjacent to the medial commissure showed no endothelization. Immediately after operation the hemolysis ceased.

Patient 2

A 25-year-old woman was admitted with congestive heart failure to an outside hospital. She had a history of rheumatic fever, but before this hospitalization she reported only mild dyspnea on exertion. A Doppler echocardiogram showed mitral stenosis with estimated valve area of 2.6 cm^2 and severe mitral regurgitation. Cardiac catheterization demonstrated mitral stenosis with an estimated valve area of 2.5 cm^2 and 3+ mitral regurgitation. The coronary arteries were normal.

Mitral valve repair by placement of a No. 29 Duran annuloplasty ring was undertaken. After placement of the ring, an intraoperative Doppler echocardiogram showed that mitral regurgitation was still present but it was believed to have been markedly improved.

Immediately after operation, the patient had severe hemolysis with gross hemoglobinuria, and her hemoglobin level fell from 0.098 g/L (0.0098 g/dL) to 0.064 g/L (0.0064 g/dL) over a period of 5 days. The haptoglobin level was low, and the lactic dehydrogenase and bilirubin levels were elevated. Schistocytes were present on the peripheral smear. The patient underwent a second repair of the valve. Inspection showed that although the annuloplasty ring was well seated, it did not provide mitral competence. It was replaced with a smaller (26-mm Car-

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pentier Edwards) annuloplasty ring. After the second operation, residual regurgitation was eliminated and the hemolysis ceased.

Comment

Intravascular hemolysis has been reported in a variety of postoperative settings: after placement of prosthetic patches for repair of congenital defects [8], with various mechanical valves [2], and with paraprosthetic leaks [3]. We are aware of only 4 other patients in whom hemolysis was reported in association with mitral valve repair [7, 9, 10], of which only 1 patient had placement of an annuloplasty ring. Hemolysis has been said to be a marker for ring dehiscence [10]. Our 2 patients demonstrate that intravascular hemolysis can occur in association with cloth-covered rings that are appropriately seated. We suggest that whenever a regurgitant jet of sufficient velocity hits a prosthetic device, hemolysis may occur. This may occur even in the presence of an adequate repair, as in our first patient. The possibility of severe hemolysis as a consequence of incomplete repair should make surgeons wary of accepting anything less than the most trivial mitral regurgitation as an acceptable result after an operative repair. Alternatives such as suture techniques for decreasing the valve orifice size avoid the use of a cloth-covered ring and may be useful in preventing this complication.

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Extended En Bloc Resection of a Primary Mediastinal Parathyroid Carcinoma

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Parathyroid carcinoma is a rare endocrine tumor infrequently seen in the mediastinum. This report describes a patient who underwent en bloc resection of a primary mediastinal parathyroid carcinoma. The tumor originated from the thymus and extended from the aortic arch to the thyroid; local invasion suggested malignancy. En bloc resection of this carcinoma with all surrounding tissue provided local control of the tumor and relief of symptomatic hypercalcemia.

(Ann Thorac Surg 1990;50:138–40)

Two percent of normal parathyroid glands are located in the superior mediastinum [1] and often are contained within the thymus. Primary parathyroid carcinoma (PC) has been rarely described in this location and often ineffectively treated with chemotherapy or radiation therapy. Surgical resection of cervical PC [2] and even isolated foci of metastases [2, 3] has provided patients with optimal local control, attenuation of hypercalcemia, prolonged disease-free survival, and occasionally cure. Regardless of location, the surgical treatment of primary PC should be complete resection of all parathyroid-containing tissue at the first operation. This report describes a patient who had primary PC of the mediastinum and underwent an extended en bloc resection of his tumor. He remains disease free with normal serum calcium and parathyroid hormone levels at 9 months.

Progressive shortness of breath, hoarseness, severe dysphagia, and a neck mass developed in a previously healthy 47-year-old man over 6 months. On examination, the mass extended from the inferior portion of the thyroid cartilage to below the thoracic inlet and laterally to the anterior border of each sternocleidomastoid muscle. The mass was not pulsatile and did not produce an audible bruit. The left vocal cord was paralyzed. The remainder of the patient's physical examination was normal. His past medical and surgical history was unremarkable. A chest roentgenogram (Fig 1) demonstrated an anterior and central mediastinal mass compressing the trachea extending through the thoracic inlet. Serum calcium level was 4.38 mmol/L (17.6 mg/dL) and decreased with hydration and diuretics to 2.8 mmol/L (11.3 mg/dL). The level of immunoreactive C-terminal parathyroid hormone was 6,500 pg/mL (normal, <50 to 350 pg/mL). A chest computed tomographic scan (Fig 2) showed a superior mediastinal mass extending from the inferior border of the thyroid posteriorly to each side of the trachea and inferiorly to the level of the aortic arch. The tumor abutted the right posterolateral half of the trachea and the right main bronchus causing substantial narrowing of the trachea. No serious mediastinal or hilar adenopathy was noted. A barium swallow demonstrated displacement of the cervical esophagus to the right. No esophageal mucosal abnormalities were noted. A thyroid scan, bone scan, and computed tomographic scan of the abdomen were normal.

An incisional biopsy of the mass revealed PC. Immunoperoxidase studies showed immunoreactivity for parathyroid hormone and chromogranin in neoplastic cells. Broad bands of dense fibrosis and an infiltrative growth pattern were indicative of PC; however, mitotic activity and vascular invasion were lacking. A bilateral neck exploration and en bloc resection encompassing thyroid, thymus, and a large anterior mediastinal PC was performed through a collar incision and median sternotomy (Fig 3). The mass was cystic and multilobulated, and appeared to arise from the thymus gland. The mass extended from the aortic arch to the thyroid gland and surrounded the anterior three quarters of the trachea. The left recurrent laryngeal nerve was encased with tumor and was removed; the right recurrent laryngeal nerve was displaced laterally in the neck but was free from tumor.

Histological study (Fig 4) demonstrated a diffusely infiltrative tumor composed of islands and trabecula of cytologically bland cells with clear cytoplasm. Broad bands of sclerotic connective tissue were associated with the infiltration. No mitotic activity or vascular invasion was observed. Two lymph nodes were free of metastatic disease. All margins were tumor free.

Postoperatively serum calcium level dropped to a nadir

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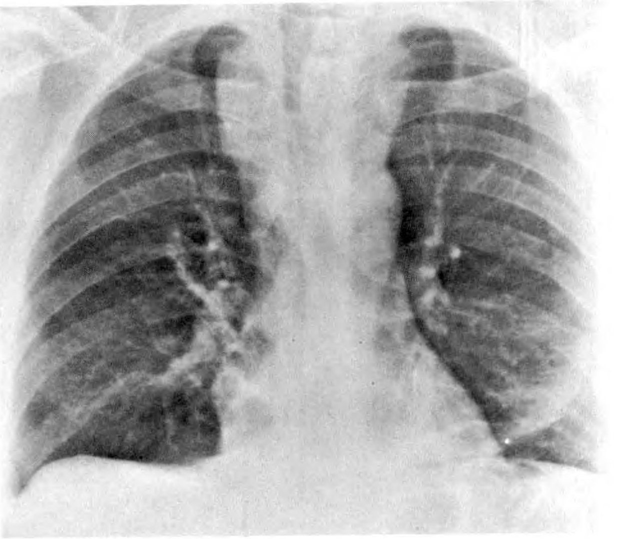

Fig 1. Chest roentgenogram showing a large mediastinal mass extending to the thoracic inlet. Compression of the trachea is noted.

of 1.86 mmol/L (7.5 mg/dL) and increased to 2.19 mmol/L (8.8 mg/dL) with oral calcium supplementation before discharge. The patient's postoperative immunoreactive C-terminal parathyroid hormone level was 230 pg/mL. He was discharged after 8 days on a daily regimen of 0.15 mg of oral thyroxine. The patient underwent prophylactic mediastinal irradiation (60 Gy over 6 weeks) and is alive and well 8 months after his operation. Currently his immunoreactive C-terminal parathyroid hormone level is 170 pg/mL (N-terminal parathyroid hormone, 11 pg/mL [normal range for men, 4.0 to 19.0 pg/mL]; pancreatic polypeptide, 40 pg/mL [normal range, 0.0 to 150 pg/mL]); and the level of serum calcium is 2.16 mmol/L (8.7 mg/dL) with no calcium supplements.

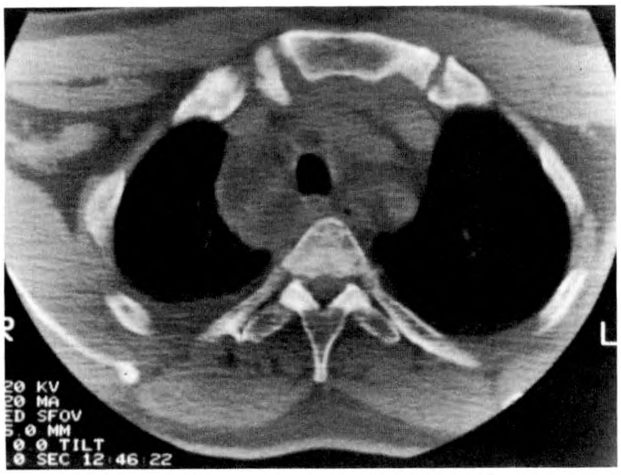

Fig 2. Computed tomographic scan of the upper thorax at the level of the sternal notch. A large contrast-enhancing lobulated multicystic mass obliterates the anterior mediastinum, encircles the trachea, and partially obstructs the esophagus.

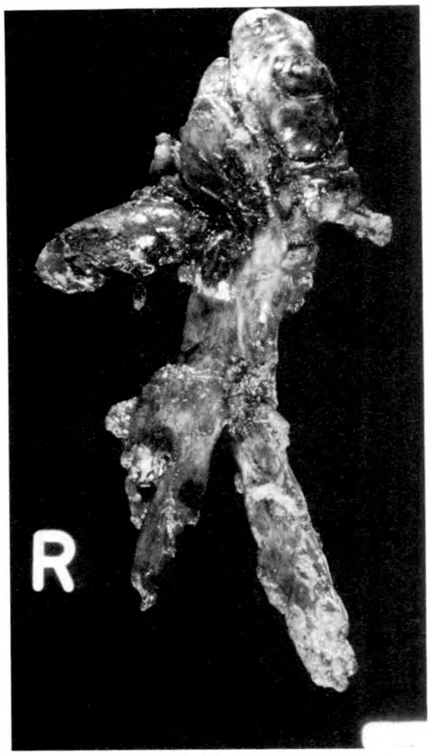

Fig 3. Resected specimen. Fibroadipose tissue was infiltrated by a solid and multicystic grey-tan tumor that extended to the aortic arch. The cysts were focally lined by blunt papillary projections and contained hemorrhagic fluid. The thyroid was unremarkable and the thymus, atrophic.

Comment

The best treatment of primary PC remains surgical resection [2]. Isolated metastases also may be resected to enhance survival and control hypercalcemia [2, 3]; multiple metastases may not be as amenable to surgical resection. Chemotherapy and irradiation alone or as adjuvant therapy are often ineffective in controlling symptomatic hypercalcemia from unresectable primary PC or metastases [3].

Parathyroid carcinoma within the mediastinum is not frequently observed. Kastan and colleagues [4] described a 57-year-old woman with a fifth supernumerary parathyroid gland carcinoma identified as a mediastinal mass that was successfully resected through a sternotomy. Hypercalcemia and increased parathyroid hormone levels had persisted despite prior neck exploration with 3½ normal parathyroid glands removed. Murphy and co-workers [5] described a 51-year-old man who had a nonfunctional parathyroid carcinoma (normal levels of immunoreactive C-terminal parathyroid hormone, calcium, phosphorus, and creatinine) with a large mediastinal mass. Exploration demonstrated the tumor adherent to the esophagus and the trachea. After treatment with radiation therapy (50 Gy in 20 treatments) and chemotherapy (cyclophosphamide, methotrexate, mitoxandrone, and lomustine), some improvement was noted.

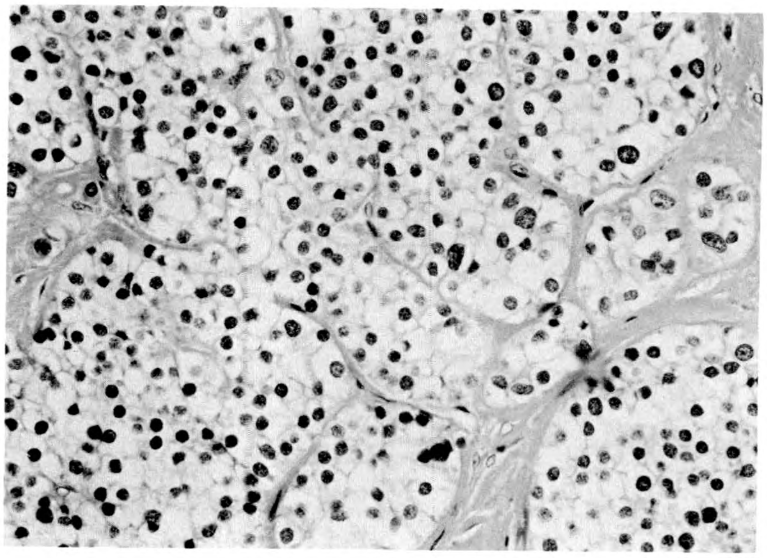

Fig 4. Hematoxylin and eosin preparation of resected specimen. High-power magnification demonstrates nests of clear cells showing focal anisonucleosis but no mitotic activity. Associated bands of sclerotic connective tissue are present.

In our patient, the tumor was malignant as demonstrated by its invasive clinical characteristics at operation. The central thymic location of the tumor and its extension inferiorly to the aortic arch and superiorly to the thoracic inlet support the anterior mediastinum as the originating site of this neoplasm.

The principles of resection of primary PC are constant whether the tumor is limited in location to the neck, to the thorax, or as isolated metastases. En bloc resection of PC with histologically confirmed tumor-free margins provides the patient's best chance for cure. Despite large, bulky intrathoracic disease, aggressive resection with wide local excision of this mediastinal PC has provided substantial palliation and disease-free survival to this patient.

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Right Atrial Perforation by a Temporary Epicardial Pacing Wire

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Cardiac perforation by an epicardial pacing wire is an extremely rare event. A case of right atrial perforation occurring 10 hours after coronary artery bypass grafting is reported. Another cause of bleeding and cardiac tamponade after cardiac operation is therefore illustrated.

(Ann Thorac Surg 1990;50:141–2)

Temporary atrial or ventricular pacing wires are often applied to the epicardium during cardiac operations [1]. They are placed in position to aid in the management of various arrhythmias and heart block or as a prophylactic measure should these problems develop during the postoperative period. The atria or ventricles alone or both chambers sequentially may be paced through unipolar or bipolar wires. Few problems have been reported with this form of cardiac pacing.

We report a case of right atrial perforation by a temporary bipolar epicardial pacing wire that occurred 10 hours after the completion of coronary artery bypass grafting.

A 67-year-old man with increasing angina pectoris due to triple-vessel coronary disease underwent coronary artery bypass grafting in February 1989. The patient's left internal mammary artery was grafted to the left anterior descending coronary artery, and reversed saphenous vein was grafted to the obtuse marginal and posterior descending arteries.

The patient was weaned off cardiopulmonary bypass with ease. His rhythm was sinus but relatively slow at 50 to 60 beats/min. A Westmed bipolar pacing wire (Westmed International Ltd, Osborne Park, Western Australia; Fig 1) was placed on the right atrium for atrial pacing to increase his heart rate. The coil was placed in position just below, lateral to, and posterior to the tied off portion of the right atrial appendage after the venous cannula was removed.

The rest of the procedure was routine and the patient was transferred to the postoperative intensive care ward for monitoring. The initial postoperative course was uneventful with sinus rhythm, normal blood pressure, and small amounts of mediastinal drainage (25 to 50 mL/h).

Ten hours after completion of the operation, the patient began to bleed in increasing amounts from his mediastinal drainage tubes. This was associated with systemic hypotension and a reduction in his urinary output. A sharp rise in right atrial pressure from 8 to 20 mm Hg was noted. The pulmonary artery wedge pressure remained at 14 mm Hg. A diagnosis of right atrial tamponade was made, and the patient was returned to the operating theater for reexploration.

The sternotomy was reopened, and widespread ooze was noted from the extrapleural tissues. On reopening the pericardium, a large amount of blood clot and blood, approximately 300 mL, was found overlying and tamponading the right atrium. The clot was removed, exposing the bipolar epicardial pacing wire. The distal electrode had perforated a thin segment of the right atrial wall leaving a 1- to 2-mm hole from which there was brisk bleeding. Opposite the second or proximal electrode, there was denudation and marked thinning of the right atrial wall with impending perforation or rupture (Fig 2).

The pacing wire was removed. The right atrial perforation was repaired with interrupted sutures of 6-0 Prolene (Ethicon, Somerville, NJ), and the other area of weakness was similarly reinforced. The grafts, anastomoses, and cannulation sites were all checked and were found to be intact. The left pleural space was explored and contained no retained blood or clot. Drains were placed into the left pleural space and behind the sternum, and the chest was closed in the routine fashion.

The patient's postoperative recovery was complicated by acute renal dysfunction with his serum creatinine level peaking at 500 μmol/L (5.7 mg/dL) (normal, 50 to 110 μmol/L) but subsequently returning to the normal range after 5 days. He was discharged home on the 11th postoperative day.

Comment

Reported complications of temporary epicardial pacing include the infection [2, 3] and migration [4] of retained wires and hemopericardium on wire removal [5]. We now report early postoperative bleeding related to the use of temporary pacing wires.

The Westmed bipolar pacing coil was designed and developed to sit on or against the epicardial surface of the heart. Normally, for atrial pacing, the coil sits against the lateral wall of the right atrium, between it and the pericardium laterally. For ventricular pacing, the coil lies against the inferior wall of the right ventricle, between it and the diaphragmatic pericardium. Good pacing and threshold characteristics have been obtained in these positions. A theoretical advantage is that the Westmed

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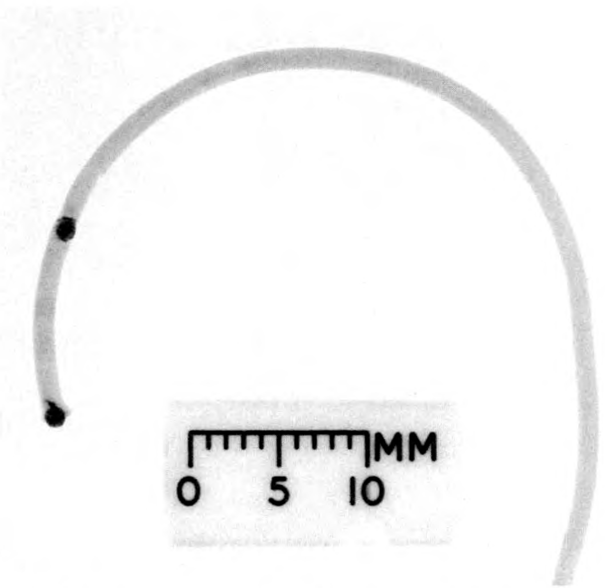

Fig 1. *The Westmed temporary bipolar epicardial pacing coil.*

pacing coil does not have to penetrate the myocardial tissue to make contact.

We have confirmed the good pacing characteristics, but migration out of desired locations may occur with the potential problem of losing pacing contact or interfering with a graft. Usually the pacing coil is sutured to the parietal pericardium opposite the site of desired contact to maintain position.

In this case, the pacing coil was placed against the right atrial wall to ensure that good myocardial contact was maintained by the two electrodes with a low threshold. The distal electrode eroded through a thin portion of atrium and the proximal electrode had markedly denuded the surface of the right atrium with impending perforation of this site too. This complication occurred as a delayed event in the early postoperative period with the onset of heavy bleeding 10 hours after operation.

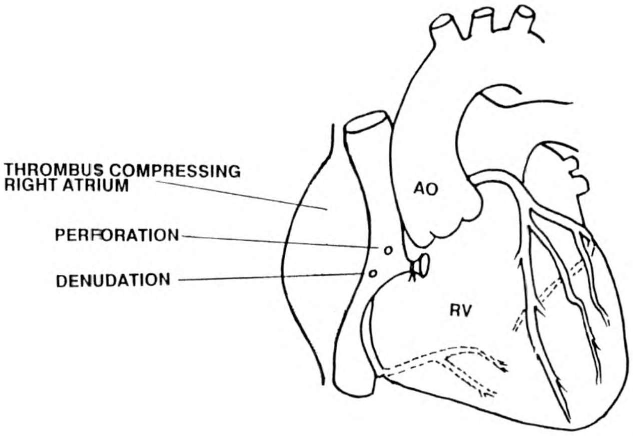

Fig 2. *The right atrial perforation and denudation with associated thrombus tamponading the chamber.* (AO = *aorta;* RV = *right ventricle.*)

Thus far, we have used over 150 Westmed temporary pacing coils without any complications. Subsequent to this case, we warn against placing the coil close or opposite to excessively thin areas of atrial wall if the coil is to be used for atrial pacing.

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Use of Glue Without Graft Replacement for Type A Dissections: A New Surgical Technique

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A new surgical technique for treating type A aortic dissections is described. It consists of the exclusive and extensive use of surgical glue without replacing a segment of the ascending aorta. Since 1984, 21 patients were operated on using this technique. No operative mortality occurred and one reoperation for redissection was required. The technique is simple and safe and yields excellent short-term and long-term results.

(Ann Thorac Surg 1990;50:143–5)

The introduction of surgical glue (gelatin-resorcin-formalin) in the treatment of ascending thoracic aortic dissection by Guilmet and co-workers [1] constitutes an important advance in the surgical treatment of this disease. In fact, surgical glue offers reinforcement of tissues, which become tough and resistant, allowing the Dacron tube to be sutured without tissue disintegration and avoiding major intraoperative or postoperative hemorrhage. We have used surgical glue at Hôpital Broussais since 1981, and we were very satisfied with the quality of tissue reinforcement and resistance it offered. In 1984, we started using a new technique to treat ascending thoracic aortic dissection consisting of isolated extensive tissue gluing without prosthetic graft interposition. We hereby describe the surgical procedure.

Technique

A femoral artery is exposed and cannulated after heparinization. Median sternotomy is then performed and 2 venae cavae cannulas are inserted. Cardiopulmonary bypass is started and the patient is cooled to 18°C. The aorta is clamped and right atrial retrograde cardioplegia is injected. A longitudinal aortotomy (Fig 1) is then performed and the site of the intimal tear is inspected. The operative field is kept dry with wall suction and walled off with sponges. In the meantime three to four tubes of surgical glue are being warmed up to 37° to 40°C.

The aortic valve is then examined, and if aortic insufficiency exists the valve is replaced or resuspended depending on the surgeon's judgment. If the dissection extends to the distal transverse aortic arch or if the intimal tear is not in the proximal ascending aorta, then circulatory arrest is performed. The patient is put in the Trendelenburg position and the pump output is gradually decreased and then stopped. The aortic cross-clamp is removed and the aortotomy is prolonged onto the transverse arch (Fig 2). In case dissection extends into the descending aorta glue is injected between the dissected aortic layers and a towel is inserted into the lumen to apply both layers together. Similarly glue is also injected between both layers of the dissected aortic arch, and transverse pouches are constructed as shown in Figure 3. Vascular clamps (bulldogs) are applied on the glued aorta for about 5 minutes. The intimal tear is then sutured and the aortotomy is closed. Noteworthy is the fact that the treated aortic layers become thicker, tougher, and more resistant, thus suture lines hold well and no tearing occurs. An aortic cannula and a suction needle are then inserted in the ascending aorta. The pump is turned on and air is evacuated. The operation is terminated in a standard fashion.

The use of gelatin-resorcin-formalin glue requires certain precautions: (1) a totally dry field, (2) glue temperature between 37° and 40°C, and (3) a small quantity (0.5

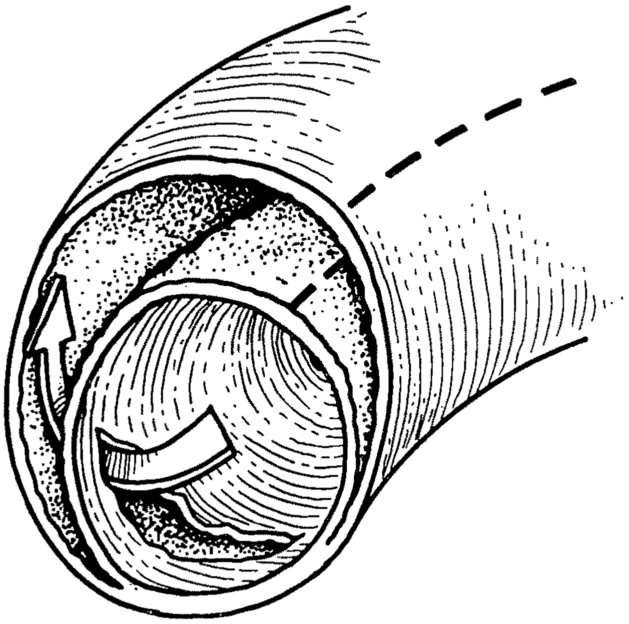

Fig 1. Longitudinal aortotomy on the ascending aorta and supracommissural intimal tear.

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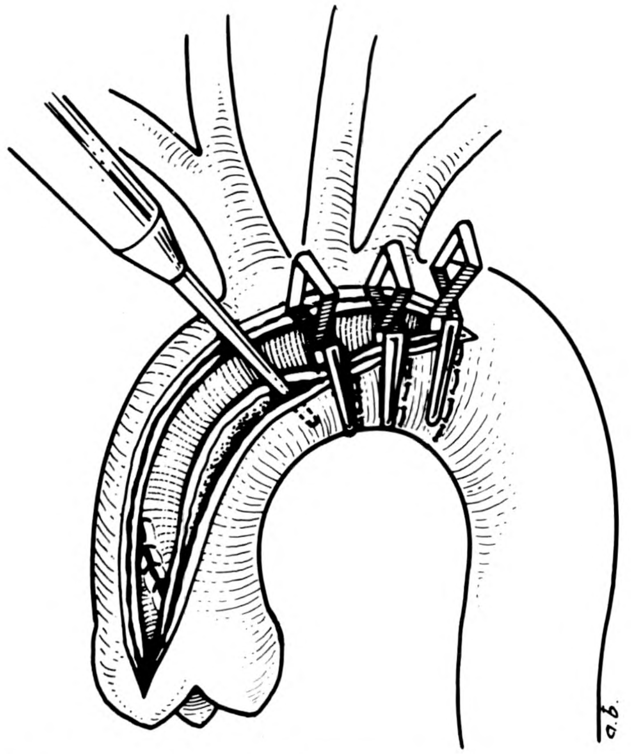

Fig 2. Aortotomy extended to the transverse aortic arch.

mL) of a polymerizing agent (formalin 9:10 and glutaraldehyde 1:10) must be added to the glue in situ and the compound thoroughly mixed (30 to 45 seconds) with a forceps to obtain a dense, adhesive, honey-like agent.

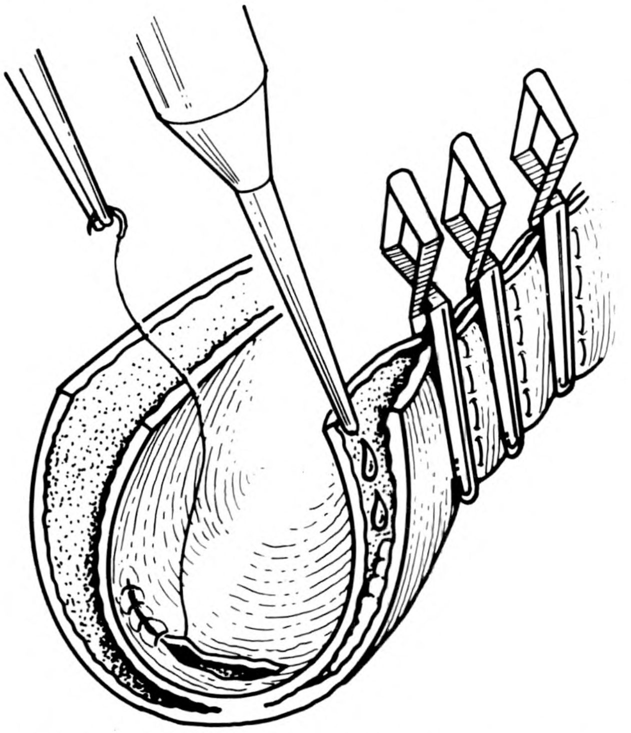

Fig 3. Gelatin-resourcin-formalin glue is injected between both layers of the aorta, transverse pouches are constructed, and clamps are applied to hold both layers together.

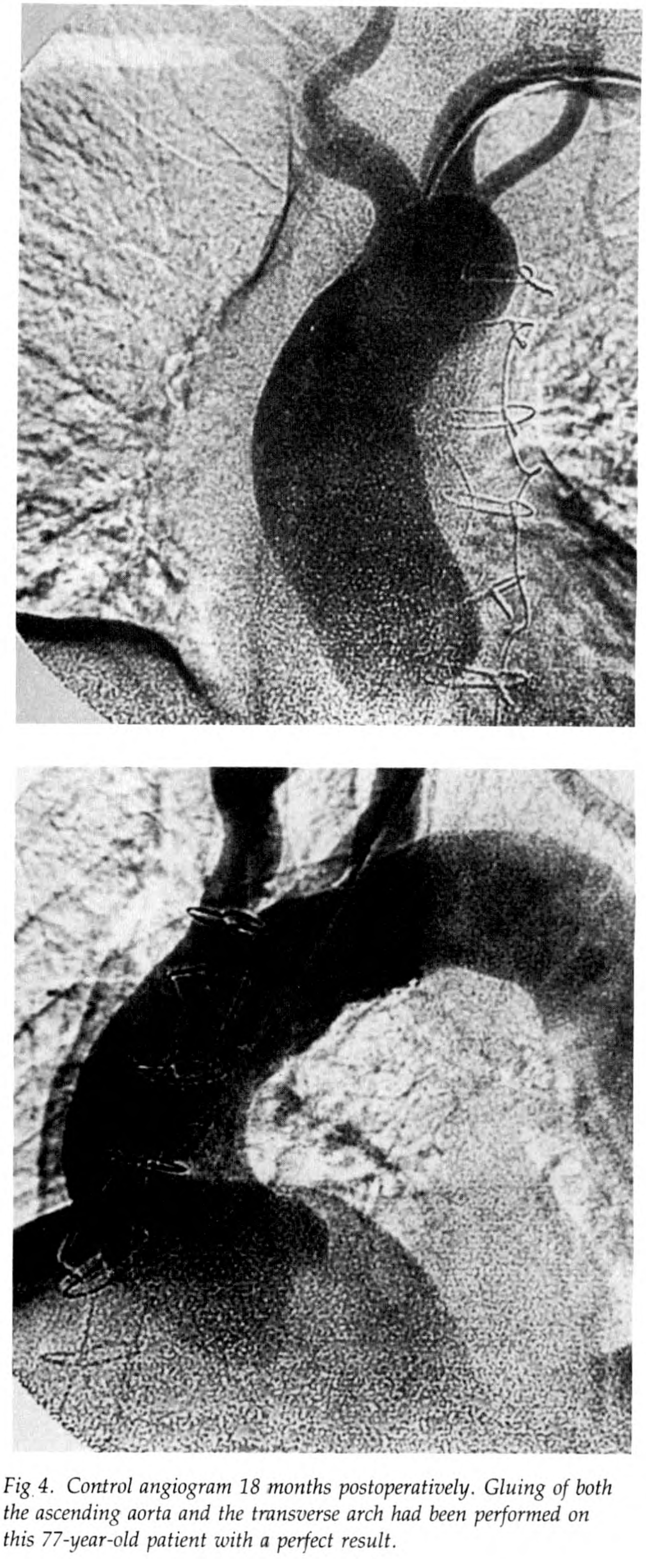

Fig 4. Control angiogram 18 months postoperatively. Gluing of both the ascending aorta and the transverse arch had been performed on this 77-year-old patient with a perfect result.

Results and Comment

Since 1984, 21 patients with ascending thoracic aortic dissection were operated on successfully using this technique, the preliminary results of whom were reported elsewhere [2]. However, of note are the following: after resumption of cardiopulmonary bypass no bleeding or redissection occurred in any case. Bleeding was not a major problem intraoperatively or in the postoperative period. Cross-clamp time ranged from 25 to 62 minutes (mean time, 42 minutes) and was significantly less than when standard repair using graft replacement was performed. No glue-related complications were noted. All patients survived and were discharged from the hospital. Follow-up was complete for all patients and ranged from 3 to 56 months. One patient required reoperation for recurrent dissection. Control angiograms (Fig 4), computed tomographic scans, and magnetic resonance imaging revealed one recurrent dissection requiring reoperation. Idiopathic cardiomyopathy developed in 1 patient 18 months after the operation and necessitated orthotopic heart transplantation. Microscopic analysis of the explanted aorta revealed good biological tolerance of the gelatin-resorcin-formalin glue as well as massive sclerosis of the aortic layers and, hence, perfect repair. Finally, in a recent case surgical glue was used with success in a similar fashion to treat a type B dissection [3].

In conclusion, the extensive use of surgical gelatin-resorcin-formalin glue without graft replacement in patients with ascending thoracic aortic dissection is a good alternative technique. It is a simple, safe, efficient method that yields good short-term and long-term results.

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Use of the Centrifugal Flow Pump for Vena Caval Shunting

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We have used the Bio-Medicus centrifugal flow pump for vena cava shunting during surgical resection of renal cell carcinoma with extension of the tumor into the inferior vena cava. The active shunt can provide optimal blood return to the heart to promote hemodynamic stability, help provide an isolated field for resection of the involved kidney and its tumor extension into the vena cava, and avoid use of full-dose heparin to minimize blood loss in this extensive operation.

(Ann Thorac Surg 1990;50:146–8)

Thoracic surgeons are frequently called upon to assist urologic surgeons performing nephrectomy for renal cell carcinoma, to facilitate removal of tumor extensions into the inferior vena cava. Tumor in the right atrium often necessitates cardiopulmonary bypass for full removal [1]. Intracaval tumor that does not extend beyond the hepatic portion of the inferior cava (group I and some group II [2]) may require venous shunting for removal if simple caval occlusion is not possible or produces unstable hemodynamics or hypotension. The centrifugal flow pump offers advantages for this shunting that make it our technique of choice for bypass during nephrectomy-cavotomy operations.

Material and Methods

Preoperatively, inferior vena cava contrast study outlines the extension of tumor into the cava. The extent of tumor cephalad and the degree of caval occlusion may help determine whether full bypass, no shunting, or vena cava to atrium shunting may be required (Fig 1).

The patient is positioned supine on the operating table

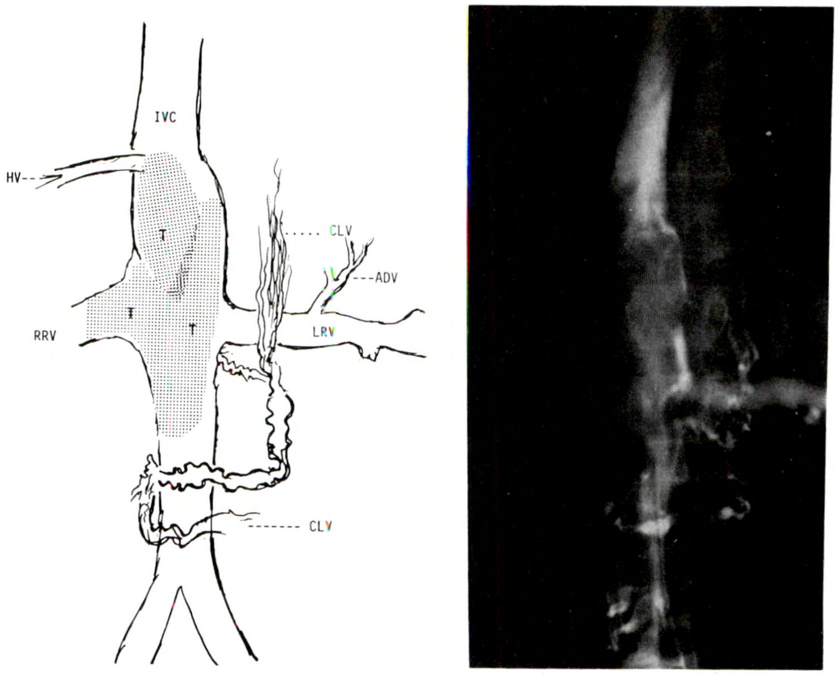

Fig 1. Vena cavogram illustrating right renal cell carcinoma with extension into inferior vena cava. (ADV = *adrenal vein;* CLV = *collateral vein;* HV = *hepatic vein;* IVC = *inferior vena cava;* LRV = *left renal vein;* RRV = *right renal vein;* T = *tumor.)*

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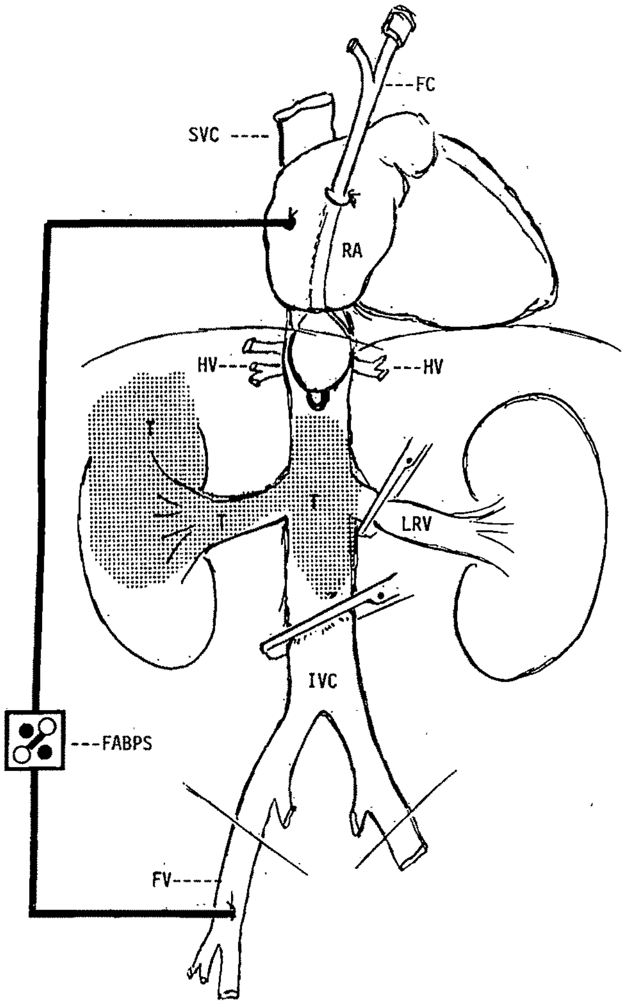

Fig 2. Operative techniques used during nephrectomy with caval extension of tumor. (FABPS = *femoral vein to atrium bypass shunt;* FC = *Foley catheter;* FV = *femoral vein;* HV = *hepatic vein;* IVC = *inferior vena cava;* LRV = *left renal vein;* RA = *right atrium;* SVC = *superior vena cava;* T = *tumor.)*

with full hemodynamic monitoring. The abdomen is opened in the midline and the duodenum and colon are mobilized to provide access to the involved kidney and cava to confirm resectability. Before manipulation of the kidney, a midline sternotomy is performed and the pericardium is opened. A pursestring suture is placed in the right atrium. The intrapericardial vena cava is encircled with a tape. A common femoral vein (or infrarenal vena cava if uninvolved with tumor) is exposed. A 16F venous cannula (USCI-Bard type 1856; Billerica, MA) is placed through a pursestring suture into the right atrium, and a number 20F venous cannula (USCI-Bard type 1856) is placed into the femoral vein or vena cava. These are connected to the primed centrifugal pump. Low flow of 200 to 400 mL/min is commenced (Fig 2). Low-dose heparin, with maintenance of activated coagulation time at 200 seconds, may be used if concern exists about flow through the centrifugal pump.

After the involved kidney has been mobilized, vascular control is gained. The inferior vena cava below the renal vein caval tumor is encircled. If inadequate space below the liver is available for controlling or encircling the infrahepatic cava, a balloon catheter is placed through the right atrium into the hepatic vena cava and the vena cava can be occluded by inflation of the balloon. This will prevent retrograde hepatic flow into the field, help prevent tumor embolism, and may avoid the need to clamp the porta hepatis. Careful placement is required above the tumor to avoid traumatization of the friable tissue mass. With the vena cava completely occluded, flow can be increased through the centrifugal pump to maintain adequate venous return, central venous pressure, and cardiac output. In most instances the flow varies between 400 and 1,500 mL/min, depending on the preexisting flow through the vena cava that is partially occluded by tumor.

When the kidney is ready for removal, the opposite renal vein is occluded to prevent tumor dislodgement into it. The renal artery and the ureter are transected. The inferior vena cava in the region of the tumor is opened and the tumor with caval extension is removed en bloc. If tumor is adherent to the involved renal vein, a button of vein can be removed from the inferior vena cava wall and the defect reconstituted with autologous vein, pericardium, or synthetic material. After closure of the vena cava incision, vascular occlusions are released and the centrifugal pump is weaned off and removed.

Comment

Renal cell carcinoma extension into the vena cava exists in up to 10% of patients undergoing nephrectomy [3]. It is well documented that surgical resection of the vena cava tumor with the involved kidney prolongs survival and provides potential cure in these patients [1].

In their large series, Skinner and associates [1] used a thoracoabdominal approach with excellent results. The combined midline approach was discussed in their publication, and shunting techniques were proposed for tumors whose cephalad extension in the tumor was limited. David and co-workers [4] described use of the Bio-Medicus pump in 2 patients and detailed the surgical technique. Attwood and colleagues [5] also described a right lateral approach with venous bypass, using the centrifugal pump, in 1 patient with a right-sided tumor.

The combined midline abdominal and sternotomy incision provides a wide exposure for operation, should shunting be required, and for either right or left nephrectomy. Access to the right atrium allows placement of balloon occlusive catheters during removal of the tumor. If needed, a vena cava filter can be placed through the right atrium into the inferior vena cava to prevent embolism of nonremovable blood thrombus propagated in the distal venous system below the tumor thrombus.

When full cardiopulmonary bypass for removal of tumor that extends into the right atrium is not required, use of the active centrifugal shunt provides several advantages. Full-dose heparin is not required, reducing blood loss. The active component of the shunting, in contrast to passive rerouting, allows assured control of venous return, which promotes hemodynamic stability. The shunt provides an isolated field for careful removal of tumor and caval reconstruction, not compromised by time or cardiac instability. After using passive (Gott) shunts in 2 previous patients, we have used this technique in the last 3 patients for whom we have provided assistance with vena caval shunting. Flows have ranged from 200 to 1,500 mL with bypass times from 30 to 120 minutes. In one patient, a 30-mL Foley balloon was placed through the right atrium and inflated just below the hepatic veins and above the tumor extension before manipulation of the cava. A second patient had placement of a Greenfield filter just below the remaining renal vein to prevent recurrent pulmonary emboli. All 3 patients had complete removal of tumor and were discharged well from the hospital.

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A Useful Technique for Closure of Pulmonary Lacerations

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Methods of closing lung tissue with stapling devices or simple sutures are usually adequate. In some patients lung tissue is so friable that reinforcement of the sutures with tissue flaps is beneficial. Felt bolsters or pledgets can also be used as we describe.

(Ann Thorac Surg 1990;50:149–50)

Lacerations, perforations, and resections of pulmonary tissue if not sealed properly may allow prolonged air leak and hemorrhage [1]. Currently accepted methods of closure, using stapling devices or simple sutures, occasionally fail [2, 3] and cause further lung damage [4, 5]. This is particularly true of contused or overexpanded lung. We have used felt pledgets or bolsters for reinforcing suture lines in several situations. Prolonged air leak, continued hemorrhage, or both were avoided in all patients.

Technique

Long felt (either Dacron or Teflon) bolsters are used to stabilize suturing of massively lacerated lung as shown in Figure 1. The bolster can be placed with a single running suture. Bolsters also can be sutured to each side of the laceration and a tertiary suture line used to approximate the severed lung. Nonabsorbable 3-0 sutures have been used effectively.

In addition to using this technique in traumatically induced lacerations, we have successfully employed the method to close lung after resection of giant bullae as shown in Figure 2.

Comment

The usual repair of torn or resected lung involves the use of either a mechanical stapling device or simple suturing of the disrupted tissue [2, 3]. Several examples of pulmonary pathology occur in which this technique may not be satisfactory, allowing for prolonged hemorrhage or air leak. Fibrotic lung, particularly in the patient who has been maintained on long-term steroids, may not hold sutures, leading to unsatisfactory air leak [6]. Badly contused lung resulting from penetrating or blunt trauma also is not easily amenable to simple suture methods. Likewise, the overexpanded lung encountered in bulla emphysema is difficult to close, and prolonged air leak is a recognized hazard of bleb resection [7].

The use of felt pledgets or bolsters to prevent tearing of pulmonary tissue has proved satisfactory in our practice. The method is quite simple, and because the sutures are held by the felt, the suture line is maintained without further tearing even with overexpansion of lung due to disease or mechanical ventilation.

Concern about placing foreign bodies in apposition to an open airway is real. It would be thought that the use of such material in an injured lung or patient treated by steroids would increase the incidence of empyema, particularly with prolonged air leak. However, postoperative empyema is a function of poorly drained and incompletely closed pleural spaces that allow air leaks and poor expansion of the lung [8]. Intrapleural infection has not developed in any of the patients in whom we have used felt material. Without further experience, however, it would not be recommended that this method of lung

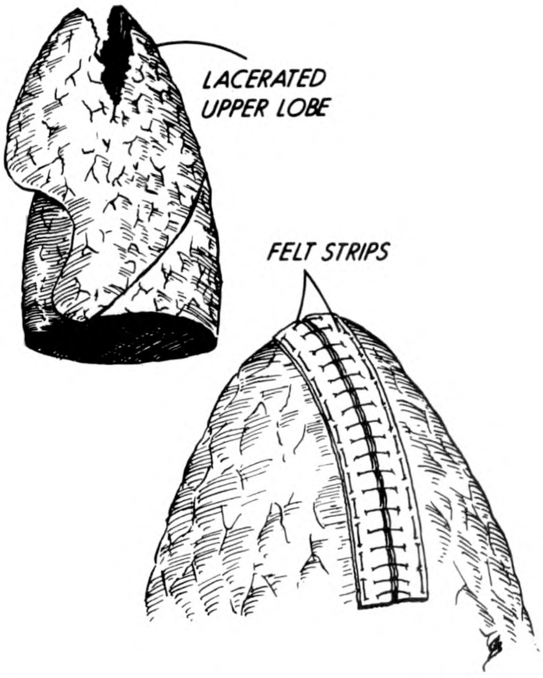

Fig 1. Repair of the severely lacerated lung with felt pledgets.

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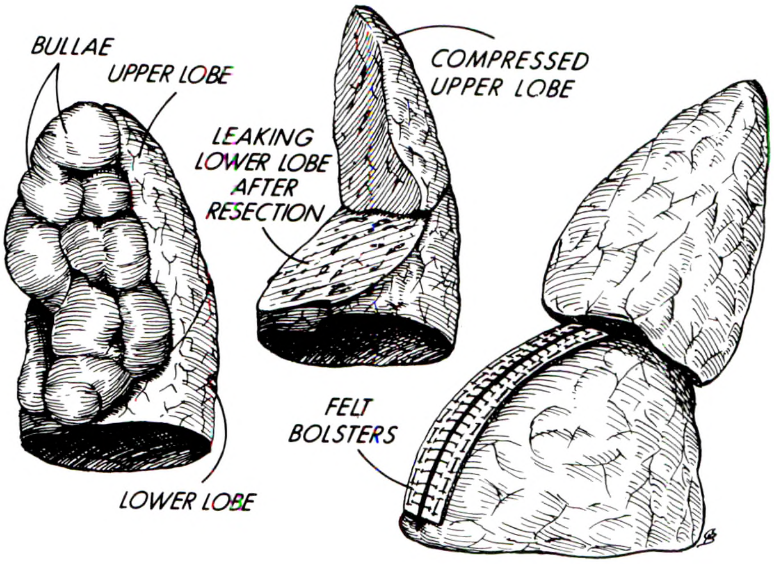
Fig 2. Resection of giant bullae with closure of lower lobe under bolsters.



closure be used in patients with pulmonary infection or long-term bronchopleural fistula.

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Development of an Artificial Heart Valve

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When I reviewed the 21-year results with the Björk-Shiley tilting disc valves, I found out that to date, we still have to use these disc valves and all mechanical heart valves with anticoagulation therapy. The highest incidence of valve-related postoperative deaths after aortic valve replacements in Stockholm was anticoagulation-related bleeding, which continued at a rate of about 1% year after year. There is a need to improve the quality of life for heart valve patients, especially for children, for young females who want to have children, for the older generation who are on medical treatment, and for all patients in whom long-term anticoagulation of a perfect quality is impossible to guarantee. A series of tests on goats has been performed, using the Björk-Shiley Monostrut valve used in 2,024 patients at the Karolinska Hospital in Stockholm and in 75,000 patients worldwide for up to 8 years with a modification of a microporous surface. In the mitral position, this modified partially microporous-surfaced Björk-Shiley Monostrut valve has permitted goats to live for 5 years with four normal pregnancies without anticoagulation therapy.

(Ann Thorac Surg 1990;50:151–4)

It is estimated that about 100,000 patients worldwide have an artificial heart valve implanted each year. These man-made heart valves are produced from various materials and of various designs. It was not so long ago that no prosthetic heart valves were available.

During the early 1950s, dilation of calcified aortic valves was the first treatment available in Sweden. I used Bailey's "Cadillac" dilator, first guided by a wire with a spherical tip, which could be palpated in the root of the aorta before the dilator was pushed through the calcific valve. The crack of the calcific valve could be heard when the dilator was opened. The dilation caused a very small change or decrease in valvar gradient, and there was usually a restenosis within 1 or 2 years. When the gradient did decrease considerably, valvar insufficiency developed. In my first 22 patients with dilation, long-term results were bad. Severe regurgitation occurred when a bicuspid aortic valve was dilated. As the results were not good, I had to be careful with the selection of patients. First, I had to develop a better procedure for exact diagnosis with catheterization of the left side of the heart before attempting further to treat calcified valves. I used an 18-cm long needle that was introduced at the upper border of the ninth rib, 2 fingerwidths to the right from the posterior midline. The needle, touching the vertebral body, then entered the left atrium. A catheter was introduced through the left atrium and passed through the left ventricle out into the aorta. On withdrawal, the pressures in all portions of the left side of the heart could be recorded.

When I had the heart-lung machine with the spinning disk oxygenator available in 1958, I started manual decalcification of the aortic cusp. This method was more effective in reducing the pressure gradient. Unfortunately, the gradients did return in 1 to 2 years.

Something more radical had to be done. I then replaced the aortic leaflets with the Bahnson Teflon cusps, sewn in "free-hand." This method resulted in calcification and cusp rupture within 1 to 2 years. In a few survivors, I could replace the Bahnson cusps with the Starr-Edwards ball valves. However, in the patients with narrow aortic roots, the Starr-Edwards ball valve (size 8A) gave a gradient of 70 mm Hg, and 6 of 8 patients died. Something better was needed.

I made aortic cusps out of the patient's own pericardium, but they wore out and ruptured within 6 months. Better results were obtained with the patient's own fascia lata. However, even the fascia lata cusp shrunk down and calcified within 4 to 5 years.

I then used the Kay-Shiley flat disc valve for aortic valve replacement. The Kay-Shiley valve gave a gradient as high as was obtained with the ball valve, but the patients with Kay-Shirley valves could tolerate tachycardia during exercise without a decrease in blood pressure better than patients with ball valves.

I went to Hokkaido, Japan, to visit Dr Juro Wada, who was using the Wada-Cutter Valve. I started using this hinged tilting disc valve and found that the gradient was substantially lower, ie, only one half of the gradient found in the Kay-Shiley valve. Later fibrin formation in the hinge caused malfunction of the occluding mechanism. The localized wear in the hinge then caused embolization of the disc. I had learned that the tilting-disc concept could diminish the pressure gradient, but the hinge had to be avoided. Donald Shiley presented his ideas of a valve with a free-floating disc (without a hinge), and with some improvements of a prototype, I immediately knew we had to try this idea. With this Delrin disc valve in the aortic position, there was a 15-year actual survival of 55% in the first 150 cases, compared with a 76% survival for Swedes of similar age and sex. After 20 years of follow-up, the Delrin disc is still functioning well in the first 14 surviving patients I have investigated.

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In 1971, the Delrin disc was exchanged with a disc of pyrolytic carbon (later called the "conical" disc). The pyrolytic carbon disc eliminated the problems associated with sterilizing the Delrin disc, which could retain water and swell, and it provided a considerable increase in durability.

In 1975, the conical disc was replaced with a spherical disc that incorporated a radiopaque marker in the disc. On screening, it was then easy to verify the function of the disc movement. (I call both the conical and spherical discs "flat" discs in contrast to the convexoconcave discs.)

In the whole group of 1,657 patients with aortic valve replacement, with Björk-Shiley valve models, the 15-year actuarial survival was 54%. Twenty-five percent of late deaths were valve related, 8.3% were mainly of anticoagulation-related bleeding, and 5.4%, of thromboembolic complications.

In 764 patients with mitral valve replacement using all models, the 15-year actuarial survival was 51% compared with 82% of healthy Swedes (matched control population of the same sex and age). The valve-related cause of death in these 764 patients was dominated by valve thrombosis in 10%, embolism in 3%, and anticoagulation-related fatal bleeding in 4%.

From the beginning, both the inflow and outflow struts were welded into the valve ring. Of 1,100 patients with a flat disc, I had one inflow strut rupture. The inflow strut was then made an integral part of the valve ring for the convexoconcave disc valve, after which no inflow strut ruptured.

The main thing was now to improve the valve flow to diminish thromboembolic complications. In 1976, I implanted the first convexoconcave disc valves, in which the configuration of the disc was changed mainly to improve the flow through the smaller flow area and thereby diminish thromboembolic complications. When open, the fluid forces would cause the disc to slide out of the orifice by 2 mm, eliminating the low-flow area caused by the disc edge touching the orifice in the earlier valve models with a flat disc. As a result of the earlier inlet strut fracture, the inlet strut was made an integral part of the convexoconcave valve ring. In 1978, the report of an outlet strut fracture was received in the United States. Then we decided that a single-piece valve, later known as the Monostrut valve, should be developed. In the mean time, the opening angle was increased from 60 degrees to 70 degrees. This change would reduce the opening forces on the outlet strut. The 70-degree opening angle was also important to avoid a vortex formation behind the smaller hole and to diminish the gradient, making the valve suitable for narrow aortic roots. During one week in March 1982, I experienced my first two outlet strut ruptures in large 70-degree mitral valves. This was a shock, and I immediately stopped using the large convexoconcave valve model and would only use the Monostrut valve.

Review of clinical results of the convexoconcave valve models, both with 60-degree and 70-degree opening angles, showed that the thromboembolic complications were reduced by 50% over the earlier models with a flat disc, with exactly the same anticoagulation treatment and identical rate of bleeding complications. At 5 years of follow-up, a 1.2% rate of thrombosis was encountered in patients with the convexoconcave disc valve in the mitral position, as compared with a 7.1% rate in patients with the earlier flat disc valves. The 2-year mortality, however, was 2% higher, mainly because of rupture of the outflow strut. The 7-year actuarial survival was 9% better, ie, 80% for patients with the convexoconcave disc as compared with 71% for patients with the earlier flat disc valve.

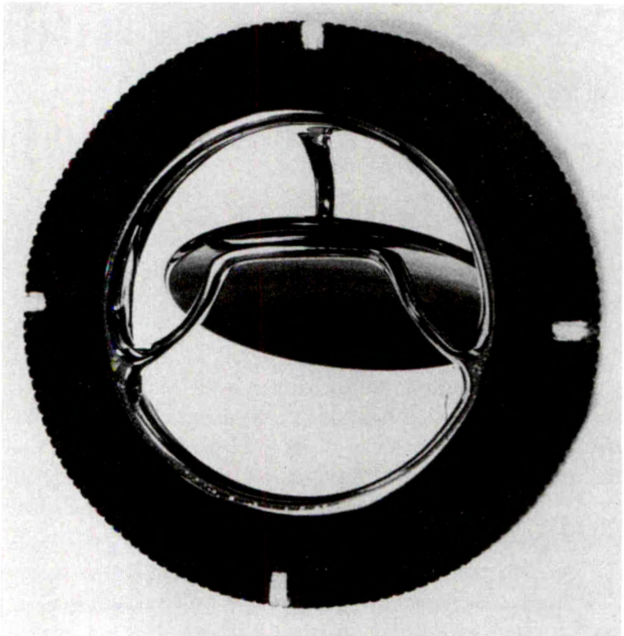

Fig 1. The Björk-Shiley Monostrut mitral heart valve with 70-degree convexoconcave disc opening. Notice the space between the edges of the disc and the valve ring as the disc slides out 2 mm in the open position.

To date, the monostrut valve has been used, without rupture, in 2,024 patients at the Karolinska Hospital in Stockholm and in more than 75,000 patients worldwide, outside the United States. The Monostrut disc opens to 70 degrees, which is important (Fig 1). There were no episodes of thrombosis or fatal embolism in our first group of patients with Björk-Shiley Monostrut valves. Detailed follow-up has shown a 1.2% embolism rate in 180 patients who had aortic valve replacement and a 3.1% embolism rate in 101 patients with mitral valve replacement. Anticoagulation-related bleeding was found in 2.2% of these patients, and proved fatal in 0.5%.

As of today, no mechanical valve can be left without anticoagulation therapy. In my first aortic valve replacement series, I left 32 patients for 12 months without anticoagulation therapy. This resulted in 15.6 thromboembolic complications per 100 patient-years. These patients had to be put back on anticoagulation therapy. In 1978, the carbon-coated sewing ring was introduced. This sewing ring was developed to reduce the tissue overgrowth in the fabric cuff and thereby maintain a smoother surface of the sewing ring. To date, the importance of the carbon-coated sewing ring has been impossible to determine owing to the small complication rate of the overall series and the limited number of both Teflon cloth sewing rings and carbon-coated Dacron cloth sewing rings.

In 1976, MacGregor and co-workers described a microporous metal coating perpetuating endothelialization on metal surfaces in the bloodstream. MacGregor and co-workers' work was tested. Microporous-surfaced rings were introduced into the superior vena cava of goats. Larger porous surfaces caused clotting, but a porosity size of 20 μm produced a thin, translucent, nonvascularized endothelialized covering (Fig 2). In 1984, 19 goats had a Monostrut valve with porous coating implanted over the entire flange surface, and 10 goats were implanted with a Monostrut valve as controls. The valves were implanted in the mitral position of the goats, as thromboembolic complications in the mitral position of humans were double those of the aortic position.

All goats were treated humanely; however, no anticoagulation therapy was provided. The goats were killed between 1 and 1½ years. All the polished Monostrut controls had a different degree of thrombosis, originating from the suture ring or growing over the groove to the valve ring. No thrombosis was attached to the polished struts. The porous metal Monostruts showed an endothelialized covering from the sewing ring to the metal orifice ring, but never over the center of the orifice where the disc seats. The struts were never completely covered. The contact area of the struts where the disc continuously seats had a tendency to build up a thrombus (37%). Additional valves were porous-coated; however, in these valves the contact areas of the struts were polished, and the valves were implanted. When explanted after 2½ years, the valves looked excellent and had no thrombus formation (Fig 3). The longest porous-coated mitral Monostrut valve implants are now 5 years. The goats are currently healthy, one goat is pregnant for the fourth time, and all goats are scheduled to be killed in the near future.

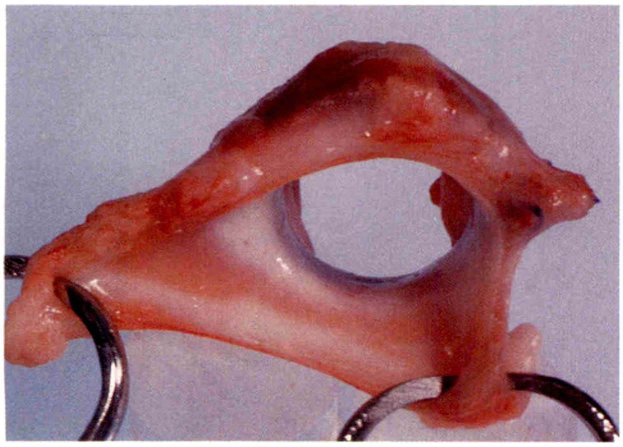

Fig 2. A valve ring of 15-mm diameter surfaced with microspheres of an average size of 20 μm inserted into the superior vena cava of a goat and explanted after 6 months when it was covered with a smooth, thin, translucent neointima continuous with the intima of the superior vena cava and the right atrium.

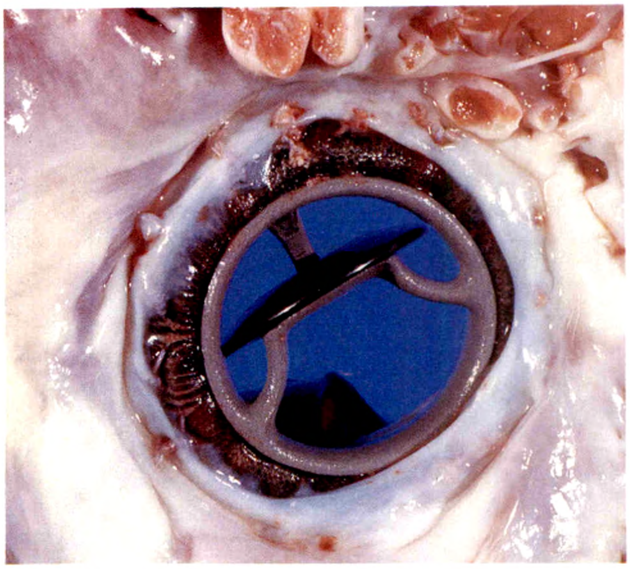

Fig 3. The modified porous-surfaced Björk-Shiley 25-mm Monostrut mitral valve after 2½ years without anticoagulation therapy in a goat (viewed from the left atrium). The carbon-coated Teflon suture ring is covered with a thin, smooth, and glistening endothelium continuing over the groove and upper part of the valve ring.

In conclusion, the porous-coated Monostrut valve should be used. I would suggest a clinical trial be initiated with the porous-coated Monostrut valve as described. Patients would have the normal anticoagulation therapy for the first 3 months, after which they should be weaned off. I would prefer to bring the patients into the hospital for 1 week to be weaned off the warfarin or dicumarol treatment during heparin administration and then discontinue heparin administration, leaving the patients without anticoagulation therapy. The incidence of emboli should be less than the incidence of anticoagulation-related bleedings. In case of an embolus, anticoagulation therapy should be started.

In the pursuit of improved quality of life for heart valve patients, a clinical investigation of the porous-coated Monostrut valve has to be done. This is a definite step forward, and it is especially needed for children, for young females who want to have children, for the older generation who are on medical treatments that do not allow anticoagulation drugs, for patients with sickle-cell anemia, and for all patients in whom long-term anticoagulation of a perfect quality is impossible to guarantee.

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Mid-Descending Aortic Traumatic Aneurysms

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Two patients with traumatic rupture of the mid-descending aorta successfully repaired are presented. Most clinical series of aortic tears do not include this entity. A review of the world literature reveals only 9 previous cases. In 6 of the 11 patients the diagnosis was either missed or delayed. In 4 patients the diagnosis was delayed or missed because of the absence of a superior mediastinal hematoma, and in 2 patients the diagnosis was delayed because of inadequate (single-plane) aortography. Suspicion may be lacking because of absence of the upper mediastinal hematoma considered to be the sine qua non for the diagnosis of aortic rupture. Although deceleration is considered to be the mechanism of injury in tears at the isthmus, severe hyperextension (often associated with fracture dislocation of the underlying thoracic vertebra) is considered to be the causative factor in descending aortic tears. Experience with the 2 patients presented here demonstrates that a high index of suspicion and complete two-plane aortography is required to avoid the potential for catastrophic outcome subsequent to overlooking a tear of the mid-descending aorta.

(Ann Thorac Surg 1990;50:155–60)

In contrast to the massive literature that has developed pertaining to traumatic aneurysms of the aorta at the level of the isthmus, little has been written concerning traumatic aneurysms of the mid-descending thoracic aorta. Encounters with 2 such patients within 4 days prompted us to review this rare entity. The purpose of this communication is to report the unique features in diagnosis, mechanism of injury, and frequency of aortic trauma at the level of the mid-descending aorta.

Case Reports

Patient 1

A 25-year-old driver of a high-speed motor vehicle accident was admitted to the shock-trauma unit with an open depressed skull fracture, multiple lacerations, fractured ribs, and extremity fractures. Vital signs were stable and the blood pressure was 172/80 mm Hg. The chest roentgenogram on admission was interpreted as negative for widened mediastinum. A computed tomogram of the chest (Fig 1A) was obtained, and the patient was taken to the operating room for repair of his skull fracture. The following morning the thoracic computed tomogram was reviewed and interpreted as demonstrating a mediastinal hematoma at the level of the arch. An aortogram was then performed, which revealed a false aneurysm at the level of T-8 (Fig 1B). At thoracotomy a hematoma was found that began at the arch and extended down the descending aorta to T-9. The entire hematoma was explored with the finding of a 20% transverse tear posteromedially at T7–8. For adequate visualization of the tear, the aorta was transected anteriorly, then the edges were debrided and reapproximated with a cross-clamp time of less than 30 minutes. The postoperative course was uneventful. The patient gradually regained consciousness and was discharged 2 months after admission.

Patient 2

A 21-year-old victim of a high-speed automobile accident arrived in the emergency room with a blood pressure of 90/50 mm Hg and pulse of 100 beats/min, breathing spontaneously at 25/min. Positive physical findings included multiple lacerations, decreased breath sounds at the right base, and tenderness over the right clavicle. A chest roentgenogram revealed a right hemopneumothorax, pulmonary contusion, and a right clavicular fracture. The mediastinum was believed to be suspicious for hematoma (Fig 2A). A computed tomogram of the abdomen revealed a nonfunctioning left kidney. Digital subtraction angiography (used in place of standard aortography to reduce contrast load because of the renal injury) was performed, which confirmed the thrombosis of the left renal artery. The angiogram was carried up to the level of the arch and was initially thought to be negative (Fig 2B). Upon review a suspicious double density at the level of the mid-descending aorta was identified. The following morning, a conventional aortogram with a cross-table lateral view was performed, which revealed a tear at the level of T7–8 (Fig 2C). At thoracotomy a hematoma was located at the region of T-7 to T-8. The laceration, which was found to be a transverse tear of 40% of the aortic circumference on the posteromedial aspect of the aorta, was repaired with direct suture with the aorta cross-clamped above and below (cross-clamp time, 20 minutes). The renal artery was not explored. The postoperative course was complicated by pulmonary insufficiency, but the patient gradually recovered and was discharged on the 30th day.

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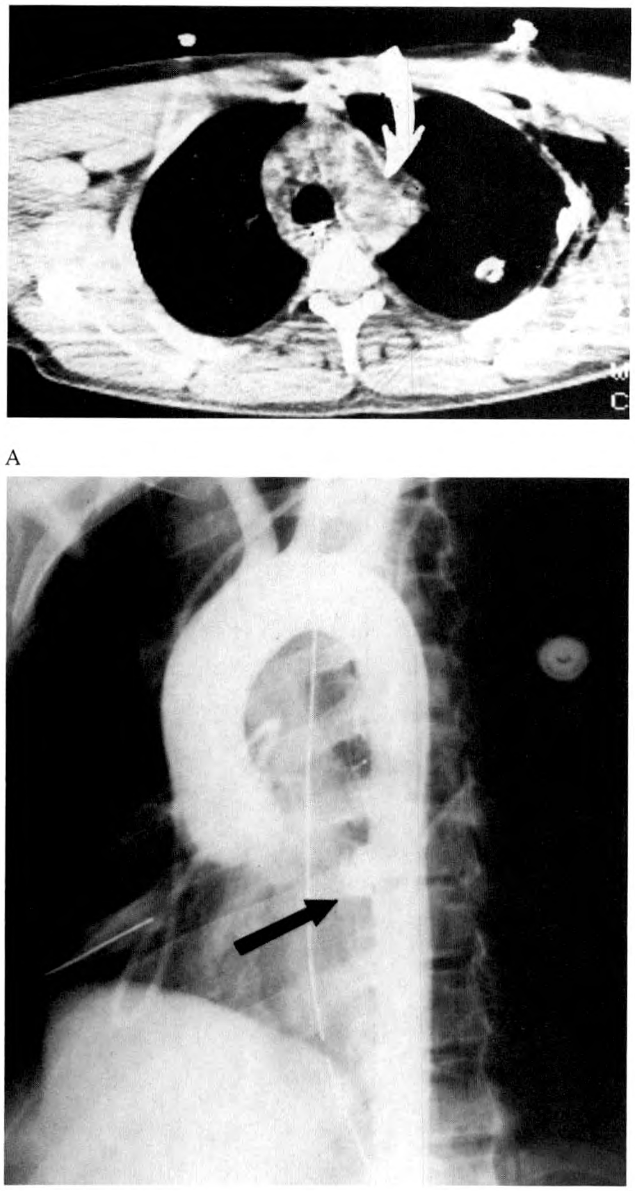

*Fig 1. (A) Computed tomogram of chest (mediastinal window). A slight thickening of the periaortic soft tissues is seen (*arrow*). At operation, this was a hematoma that extended downward from the aortic arch to T-9. (B) Thoracic aortogram reveals laceration in the posteriomedial wall of the mid-descending thoracic aorta with a false aneurysm.*

Material and Methods

Twenty-eight surgical series of aortic rupture are summarized in Table 1 and compared with a compilation of eight autopsy series (Table 2). All totals and percentages are given in reference to aortic tears only. Tears of the brachiocephalic vessels are not included. To compare the surgical series with the autopsy series the lacerations of the ascending aorta and aortic arch are combined, and lacerations of the mid-descending aorta and diaphragmatic aorta are combined in the total figures. In Table 3 we define mid-thoracic descending aorta as that segment below the region of the isthmus and above the level of the diaphragmatic aortic hiatus (T-7 to T-10).

Results

Of the 823 patients in the collected surgical series with aortic ruptures 96.7% had rupture located at the isthmus, 2.3% at the ascending aorta or arch, and only 1% at the descending aorta or diaphragmatic aorta. Of the 740 collected patients in the autopsy group only 50.4% had ruptures at the isthmus, whereas 27.2% had ruptures located at the ascending aorta through the arch and 15.7% in the descending aorta through the aortic hiatus. A total of 11 patients (including ours) were found in the literature with tears in the mid-descending aorta (defined as between T-7 and T-10).

Comment

The locations of aortic ruptures summarized from 28 surgical series of nonpenetrating aortic injury in Table 1 contrast dramatically with those derived from autopsy series (see Table 2). The incidence of isthmus lesions is much more frequent (96.7%) in the clinical series than that (50.4%) compiled from the autopsy series. When tears of the brachiocephalic vessels are included, lesions of the isthmus comprise 89% to 91.5% of the clinical series [2, 37].

Of particular interest is the 15.7% incidence of descending aortic injuries in the autopsy data as compared with a 1% incidence in the surgical series. This raises the obvious question as to whether this lesion is frequently overlooked. The autopsy series as reported do not specify whether the autopsies were performed strictly on patients seen dead on arrival or on some victims with delayed rupture.

As would be expected, the incidence of multiple ruptures is much higher in the autopsy series as compared with the surgical series (7.8% versus 1%).

A clue as to the disparity in incidence of the mid-descending aortic ruptures between the autopsied patients and surgical patients may be attributed to the mechanism of injury. It is generally agreed that the mechanism of injury in ruptures of the mid-descending aorta involve direct trauma to the aorta, viz, extreme hyperextension of the spine (with the spine actually pressing forward and shearing the aorta) or injury secondary to fracture dislocation of the adjacent spine [34]. These mechanisms are said to account for the fact that all lacerations of the mid-descending aorta are transverse [34]. We note, however, that in only 1 of the 11 clinical patients with this lesion was there an associated dislocation of the spine. In contradistinction to the apparently more direct trauma required for this injury, the trauma required to tear the aorta at the isthmus is thought to be indirect from acute deceleration phenomena [28, 34, 35].

In Table 3 it can be seen that in 6 of the 11 accumulated patients with mid-descending aortic tears the diagnosis was initially missed. In 4 of these cases the mediastinum was believed to be negative on routine chest roentgeno-

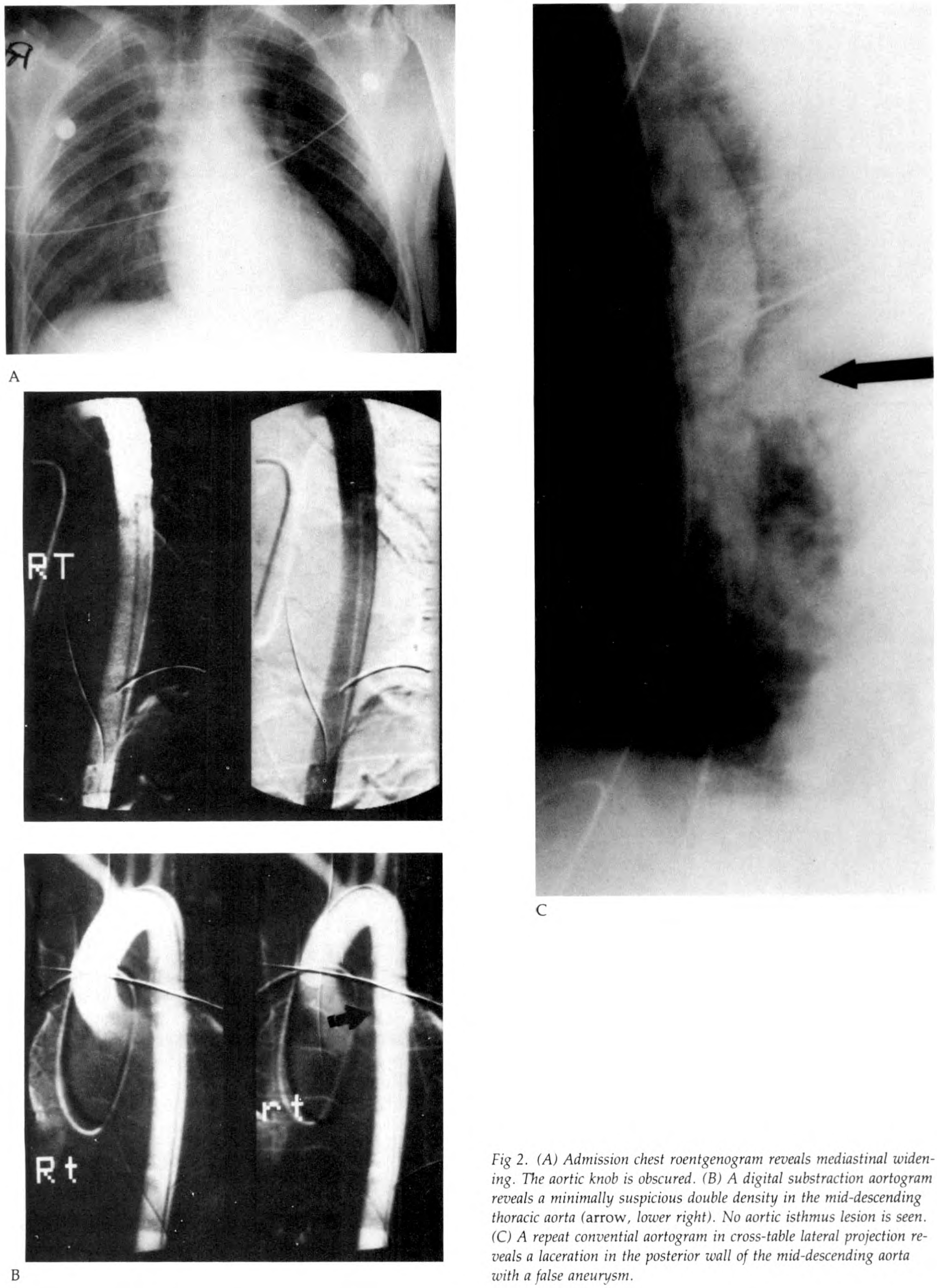

Fig 2. (A) Admission chest roentgenogram reveals mediastinal widening. The aortic knob is obscured. (B) A digital substraction aortogram reveals a minimally suspicious double density in the mid-descending thoracic aorta (arrow, *lower right). No aortic isthmus lesion is seen. (C) A repeat convential aortogram in cross-table lateral projection reveals a laceration in the posterior wall of the mid-descending aorta with a false aneurysm.*

Table 1. Site of Aortic Rupture in Surgical Series

Author	Year	Isthmus	ASCD	Arch	DESC	DIAPH	Branches	Comments
Keen [1]	1972	16	. . .	. . .	. . .	. . .	3	2 innominate, 1 subclavian
Thevenet [2]	1975	65	1	1	. . .	. . .	5	Acute tears only
Appelbaum et al [3]	1976	17	1	. . .	. . .	. . .	. . .	
Bodily et al [4]	1977	39	. . .	. . .	. . .	. . .	. . .	3 multiple; also reference [5]
Ayella et al [6]	1977	35	. . .	. . .	. . .	. . .	. . .	1 multiple
Kirsh et al [7]	1978	50	2	. . .	1	. . .	5	2 innominate, 3 subclavian
Pezzela et al [8]	1978	11	1	1	. . .	. . .	. . .	Associated aortic root injury
Plume and DeWeese [9]	1979	14	. . .	. . .	1	. . .	. . .	
Avery et al [10]	1979	10	. . .	. . .	. . .	. . .	. . .	
Akins et al [11]	1980	42	1	1	. . .	. . .	. . .	
Williams et al [12]	1980	30	. . .	. . .	. . .	. . .	2	2 innominate
Motin et al [13]	1980	32	2	1	1	. . .	. . .	
Ketonen et al [14]	1980	17	. . .	. . .	. . .	. . .	. . .	
Skotnicki et al [15]	1981	21	1	. . .	. . .	. . .	. . .	
Soyer et al [16]	1981	34	1	. . .	. . .	. . .	1	1 innominate
Grande et al [17]	1984	58	. . .	. . .	. . .	. . .	. . .	
Schmidt and Jacobson [18]	1984	40	. . .	1	. . .	. . .	. . .	
Oliver et al [19]	1984	19	. . .	. . .	. . .	. . .	. . .	
Tegner et al [20]	1984	14	. . .	. . .	. . .	. . .	. . .	
Pate [21]	1985	58	. . .	. . .	. . .	. . .	. . .	
Mattox et al [22]	1985	31	. . .	1	. . .	. . .	. . .	
Stiles et al [23]	1985	16	. . .	1	. . .	. . .	2	2 innominate
Verdant et al [24]	1985	20	. . .	. . .	. . .	. . .	. . .	
Marvasti et al [25]	1986	41	. . .	. . .	. . .	. . .	. . .	
Langlois et al [26]	1987	15	1	. . .	. . .	. . .	3	3 innominate, 1 subclavian
Hartford et al [27]	1988	16	. . .	. . .	. . .	. . .	. . .	
Tribble and Crosby [28]	1988	22	. . .	. . .	1	2	. . .	(From reference [28] plus personal communication, 1989)
PGHC (present report)	1990	12	1	. . .	2	. . .	2	2 subclavian
Subtotals		796	12	7	6	2	23	
Total aorta (n = 823)		796	19[a]		8[b]			
Percent		96.7%	2.3%[a]		1%[b]			

[a] Ascending aorta + arch. [b] Descending aorta + diaphragmatic level.

ASCD = ascending aorta; Branches = brachiocephalic arteries; DESC = descending aorta; DIAPH = at diaphragmatic level; PGHC = Prince Georges Hospital Center.

gram. The actual aortic hematoma effected by the lesion may be obscured by the heart on routine chest roentgenograms. Our first case was a serendipitous aortographic finding resulting from the computed tomographic demonstration of an unsuspected mediastinal hematoma. In 2 patients the diagnosis was nearly missed because of inadequate (one-plane) aortography. These difficulties in diagnosis lead one to suspect that some tears may go undiagnosed and spontaneously heal as suggested by Stiles and Bryant [41, 42]. This postulate would account for some of the disparity between the autopsy and clinical series.

Indications for aortography in high-speed decelerating injuries should be liberal. In addition to the standard chest roentgenographic findings that suggest the need for obtaining aortography, viz, widened mediastinum, apical cap, depressed left main bronchus [43], the finding of a thoracic vertebral fracture should prompt aortography to confirm the diagnosis and to determine the site or sites of rupture. Although the role of computed tomographic scan in thoracic trauma remains controversial, we have for the past 7 years used thoracic computed tomographic scans in major thoracic trauma because of the improved diagnostic sensitivity [44, 45]. Unsuspected mediastinal hematomas diagnosed by computed tomography, as demonstrated in our initial patient, warrant aortography. Because of the relative difficulty in diagnosing traumatic tears of the mid-descending aorta, the clinician must maintain a high

Table 2. Levels of Aortic Transection in Autopsy Series

Author	Year	Total	Isthmus	ASCD	Arch	DESC	DIAPH	ABDOM	MULT	Comments
Strassman [29]	1947	61	38	8	. . .	12	. . .	3	. . .	Ruptures in one site
		11	2	6	. . .	3	. . .	. . .	11	Multiple ruptures
Parmley et el [30]	1958	171	95	17	16	27	. . .	11	5	
		104	29	47	6	6	. . .	2	12	With associated heart injury
Zeldenrust and Aartes [31]	1962	88	63	11	. . .	. . .	5	. . .	. . .	
Jensen [32]	1964	68	35	15[a]		18	. . .	. . .	. . .	Ascending and arch lesions combined
Greendyke [33]	1966	34	22	1	. . .	. . .	7	4	8	
Sevitt [34]	1977	37	25	7	. . .	. . .	5	. . .	. . .	
Gotzen et al [35]	1980	26	21	3	1	. . .	1	. . .	2	Associated with heart rupture in 5 patients
Arajarvi et al [36]	1989	140	26	36[a]		10[b]		. . .	7	Unbelted
			25	24[a]		19[b]		. . .	13	Belted
Total (n = 740)			381	198[a]		113[b]		20	58	
Percent[c]			50.4%	27.2%[a]		15.7%[b]		2.8%	7.8%	

[a] Ascending aorta + arch. [b] Descending aorta + diaphragmatic level. [c] Total percentage greater than 100% because Parmley series calculated multiple injuries as separate patients, whereas Strassman and Arajarvi counted as major injury.

ABDOM = abdominal aorta; ASCD = ascending aorta; DESC = descending aorta; DIAPH = at diaphragmatic level; MULT = multiple aortic injuries.

Table 3. Traumatic Rupture of the Mid-Descending Aorta

Author	Year	Patients	Comment
Kirsh et al [37]	1976	1/43	Descending mid-thoracic aorta—associated with fracture dislocation of thoracic spine.
Kirsh et al [7]	1978	1/58	Descending aorta just above diaphragm—negative mediastinum or loss of aortic knob.
Plume and DeWeese [9]	1979	1/15	Mid-descending aorta; associated right atrial appendage rupture.
Motin et al [13]	1980	1/36	
Fisher et al [38]	1981	2/54	T9–10. Minimal mediastinal changes on admission chest roentgenogram. Missed diagnosis.
			T7–8. Initial mediastinal hematoma obscured by cardiac silhouette.
David et al [39]	1985	1	T7–8. Delayed diagnosis due to one-plane aortogram. Hyperextension postulated.
Stothert et al [40]	1987	1	T9–10 (estimated from published aortogram). Described as just above aortic hiatus. One of two aortic tears in patient, the other at isthmus.
Tribble and Crosby [28]	1988	1/25	(From reference [28], also personal communication [1989] as to exact site.)
Present series	1990	2/17	Delayed diagnosis. No widening of mediastinum on plain roentgenogram. (See text.)
			Delayed diagnosis. Lesion missed on one-plane aortography. (See text.)

index of suspicion and obtain adequate two-plane aortography of the entire aorta to avoid missing this potentially fatal lesion.

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Cardiac Transplantation

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Interest in cardiac transplantation has grown along with cases performed and publications cited, but editorial limits have caused important works to be deleted from this list. Postoperative surveillance for rejection using nuclear magnetic resonance, proton emission, tomography, and immunologic monitoring are not included.

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Bridge to Transplantation

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CORRESPONDENCE

Computed Tomography in Selecting Patients for Mediastinoscopy

To the Editor:

I read with great interest the study by Thermann and associates [1] in which computed tomography was found a valuable selection method for mediastinoscopy. In a similar study from our institution [2] we reached different conclusions and recommended mediastinoscopy as a routine procedure in the preoperative staging of bronchial carcinoma. These results were also observed by other authors [3, 4], who concluded that computed tomography cannot select those patients who should have a mediastinoscopy because of its low sensitivity and specificity.

In the study of Thermann and associates [1], the sensitivity and specificity of computed tomography are remarkably high (89.3% and 96.2%, respectively). The inclusion in the study of 12 patients with benign lesions and, on the other hand, the exclusion of 14 patients (14.7% of the total group) who had bronchial carcinoma but did not undergo mediastinal lymphadenectomy for various reasons could introduce a certain bias. In my opinion, stratification of the results for benign and malignant disease, which was not made in the present study, could settle this issue more clearly. In this way the sensitivity and specificity of computed tomography in the staging of bronchial *carcinoma,* which is more interesting in this kind of discussion, could be quite different.

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Reply

To the Editor:

A prospective study has to follow the protocol. The protocol of our study demanded preoperative staging procedures for all patients presumed to be operable for proven *or suspected* lung cancer. Therefore, the patients who had no malignancy in the definitive histological examination were included for they underwent the same staging procedures. The results of these patients can serve as a kind of control group. Looking only at the patients with postoperatively proven carcinoma denies the problems of preoperative staging procedures (as, for example, mediastinoscopy in a patient with a benign disease).

The fact that patients were excluded for not fulfilling the protocol was a necessary part of a prospective study, where all patients admitted to the hospital were included. Patients were only evaluated when they had an intraoperative mediastinal lymph node dissection to get the most precise information about mediastinal lymph node involvement. Therefore, our protocol seems to be a good way to reduce (and not to introduce) bias.

But the main point of disagreement of the two studies is the discrepancy in the results of the two staging methods. Mediastinoscopy in the Belgian group has an extraordinarily high sensitivity of 91%, whereas in our group sensitivity is 79% [1]. On the other hand, computed tomography (CT) for mediastinal lymph nodes in the Belgian study has a sensitivity of 68% and a specificity of 57% (accuracy, 61%), which is poor. Three studies report accuracy rates between 81% and 88% [2–4]. No details are reported from the Belgian group as to who performed the evaluation of the CT scans. In our prospective study two experienced radiologists who are co-authors (R.B., E.W.) were challenged by the surgeons, sometimes repeating unclear CT examinations using the identical scanner.

We completely agree with the Belgian authors that, on the basis of their superb mediastinoscopy and their poor CT results, distrust in CT is acceptable, although their conclusion is not helpful in the single case ("a more liberal use of mediastinoscopy seems to be justified"). But as the technical aspects of computed tomography improve (and, as we hope, those of magnetic resonance imaging) and images become more precise, the accuracy of the radiologist will increase.

Therefore, we believe that our conclusions are an acceptable mid-position between the opinions of the "mediastinoscopists" and the "resectionists."

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Endoscopic Relief of Airway Obstruction

To the Editor:

We read with interest the article by Mathisen and Grillo [1] and the editorial by McElvein [2] on endoscopic relief of airway obstruction.

Mathisen and Grillo accurately describe the best technique of forceps resection during rigid bronchoscopy. We agree with them about the possibility, by such a technique, to relieve tracheobronchial obstruction with good immediate results and relatively few risks. However, we do not agree at all that this technique might be considered better than mechanical-laser associated technique.

In addition to the considerations provided by McElvein, we think that the procedure used by Mathisen and Grillo absolutely requires a skillful rigid bronchoscopist. Furthermore, forceps

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resection during rigid bronchoscopy is often accompanied by hemorrhage that, even if almost never life-threatening, generally brings management difficulties. Such a resection also lasts longer than our technique. However, the most important thing, in our opinion, is that the results of the mechanical resection persist significantly less than those obtained by mechanical-laser associated technique.

Before having a Nd-YAG laser, we performed endoscopic resections using a very similar method to the one described by Mathisen and Grillo in 52 patients. The median time between first and second treatment in 33 patients affected by bronchogenic carcinoma in whom we have not performed any other therapy was 29 days. In contrast, the median time between first and second laser treatment, not followed by any further therapy, was 89 days in a second series of 108 patients affected by the same disease.

In our opinion, therefore, the technique of Mathisen and Grillo is justifiable only as an emergency procedure and when the laser device is not available.

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2. McElvein RB. Treatment of malignant tracheobronchial obstruction. Ann Thorac Surg 1989;48:463–4.

Reply

To the Editor:

Doctor Cavaliere and Dr McElvein are recognized proponents of the laser, and both have made important contributions in this area [1, 2]. Their published results speak for themselves and document that the laser is an alternative to rigid bronchoscopy to palliate malignant airway obstruction. We agree the laser is an acceptable method of treatment but not the only one as many have now come to believe.

The rigid bronchoscope and biopsy forceps were originally designed for removal of endobronchial tumors. They have fallen out of favor primarily because surgeons have deferred endoscopies to pulmonologists, the flexible bronchoscope has superceded the rigid bronchoscope, an unfortunate misperception of a high incidence of massive hemorrhage still exists (not documented in the surgical literature), and many surgeons have an affinity for expensive, high technology.

The rigid bronchoscope has certain advantages over the laser. The technique is simple, easy, quick, and effective. We were able to palliate over 90% of our patients. Our technique allows the patient to spontaneously ventilate throughout the procedure. The health care system is spared the cost of the laser and the extra expense of fees for using the laser, which are often two to three times what is charged for bronchoscopy. Indeed, many patients are in the final stages of their disease and cost-effectiveness must be taken into account.

The greatest concern about the laser is that its use has largely gone unregulated and is rarely in the domain of the surgeon. This may lead to patients receiving palliative treatment when surgical cure is possible with bronchoplastic techniques now available. Of equally great concern is the inappropriate use of the laser to "treat or cure" certain benign tumors of the airway. Few benign tumors can actually be treated in a curative sense with the laser unless a full-thickness injury is created in the wall of the airway. This would obviously lead to complications and would represent inadequate treatment.

Doctor McElvein reports an advantage of the laser in dealing with lobar obstruction. It has always been our impression from the literature that the laser has serious limitations at the lobar level as well, but if it does not, this may represent an indication for its use. It is interesting that Cavaliere and associates [1] state, "We frequently use the rigid bronchoscope to scoop out the endoluminal mass. With neoplasms, the laser was used to coagulate the mass and after mechanical removal of the tumor, the airway wall was photocoagulated for hemostasis." It would appear from this description that the laser is not used to resect tumors but to coagulate after the rigid bronchoscope and biopsy forceps are used to core them out. We feel that hemorrhage is rarely a problem if certain guidelines are followed and that any bleeding that ensues usually ceases spontaneously and requires no further treatment. It would therefore seem that the laser is superfluous. Doctor Cavaliere and Dr Ardigó also state that airways remain patent longer with the laser. Our feeling is that the length the airway remains patent is a function of the success of irradiation or chemotherapy.

In conclusion, if the laser is to be used we believe that regulations should be developed to control its use, that surgeons should be involved somewhere along the line to ensure surgically curable patients are not being inadequately treated, and that Dr Cavaliere's expressed concern "that [our procedure] absolutely requires a skillful rigid bronchoscopist" also equally applies to those using the laser.

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Malignant Fibrous Histiocytoma

To the Editor:

We read with great interest the two case reports about malignant fibrous histiocytomas by Paterson and colleagues [1] and Guttentag and associates [2]. Recently, we saw a similar case of this disease with involvement of the descending thoracic aorta and the left lower lobe of the lung. The report has been forwarded for publication to *The Journal of Thoracic and Cardiovascular Surgery*.

In our case radiology as well as ultrasound imaging failed to differentiate between aneurysmatic and tumorous disease. This prompted us to confirm the diagnosis by needle biopsy. As we were aware of a tumor our surgical approach was radical, consisting of en bloc resection of the lower lobe and the adjacent aorta. Our patient had an uneventful recovery without any clinical or radiological sign of recurrence 9 months postoperatively.

We somewhat disagree with the opinion of Paterson and colleagues that their malignant fibrous histiocytoma might have been induced by the Dacron vascular prosthesis. In our case as well as in the case report of Guttentag and colleagues the intraaortic tumor mass grossly looked like parietal thrombus. From our point of view the similar finding described by Paterson and colleagues at their primary surgical intervention most likely was already tumor. Unfortunately, there was no histological examination.

The observations presented by Guttentag and co-workers are extraordinary interesting because in their case histological evidence of a malignant fibrous histiocytoma had been found 5 years before the aortic symptoms. Because autopsy revealed tumor in the descending thoracic aorta as well as in the left upper lobe, the right iliac crest, both adrenal glands, and the ninth vertebra, the primary origin remains uncertain. However, the 5-year interval between first appearance and fatal outcome lets us hope for a favorable prognosis for our patient.

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References

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Reply

To the Editor:

My co-authors and I wish to congratulate Drs Laas and Schmid on their successful resection of a malignant fibrous histiocytoma involving the left lower lobe and descending thoracic aorta. Although their patient appears to be free of disease 9 months postoperatively, we would advise that they closely monitor him for signs of recurrence because our own experience and that of others suggest that the presence of aortic involvement indicates an extremely poor prognosis.

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Reply

To the Editor:

Because it is not a policy of our Unit to undertake histological examination of every removed specimen, no histology was available from the original aneurysm resection. It is therefore not possible to deny the suggestion made by Drs Laas and Schmid that tumor was already present. We can only say that we have had a large experience in vascular surgery and the original specimen had all the features of an aneurysm with attached thrombus; we were in no doubt that this was the correct diagnosis. The gross pathological features at the second operation were completely different from those present at the first procedure, and we were in no doubt that on this occasion we were dealing with tumor although this was quite unexpected from the presentation.

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Polytetrafluoroethylene Posterior Annuloplasty for Mitral Regurgitation

To the Editor:

We read with interest the recent article by David and associates [1], which was an interesting study that emphasized the importance of a flexible annuloplasty ring for preservation of better left ventricular function. Discussing the article, Dr D. L. Cosgrove stated that "the ideal annuloplasty ring should be universally flexible and provide a measured plication of the annulus of the posterior leaflet only. Currently, there is no annuloplasty ring that meets these requirements . . ." For the past 4 years, we have been using a technique of mitral annuloplasty [2] that approaches the requirements expressed by Dr Cosgrove. We employed as annular prosthesis a 4-mm polytetrafluoroethylene (PTFE) tube graft of variable length (up to 6 or 7 cm). After valve procedures (leaflet resection or repair, chordal transposition or shortening), insertion of PTFE graft was performed using mattress sutures placed into the fibrous portion of the posterior annulus and extended anteriorly just beyond the anatomic commissures (Fig 1). Proper spacing of the sutures assured desirable circumferential constriction without mitral annulus distortion. The first use of a similar technique was reported in 1976 by Cooley and associates [3], but afterward it was dismissed. We have used PTFE posterior annuloplasty successfully in 58 patients undergoing operations for nonrheumatic mitral regurgitation. All patients but 2 had clinical and echocardiographic follow-up (1 to 50 months; mean, 22 months).

In our opinion, this type of annuloplasty presents several

Table 1. Polytetrafluoroethylene Annuloplasty: Postoperative Echocardiographic Data in 56 Patients

Variable	Value
Mitral valve area (cm^2)	3.01 ± 0.37
Transmitral flow	
Velocity (m/s)[a]	1.1 ± 0.37 (0.9 ± 0.3)
E/A ratio[a,b]	0.98 ± 0.24 (1.3 ± 0.6)
LVOT flow velocity (m/s)[a]	1.05 ± 0.13 (0.9 ± 0.2)
Residual MR (No. of patients)	
None or mild	50
Moderate	3
Severe	3

[a] Values in parentheses are normal values. [b] Forty patients in sinus rhythm.

E/A = protodiastolic/telediastolic; LVOT = left ventricular outflow tract; MR = mitral regurgitation.

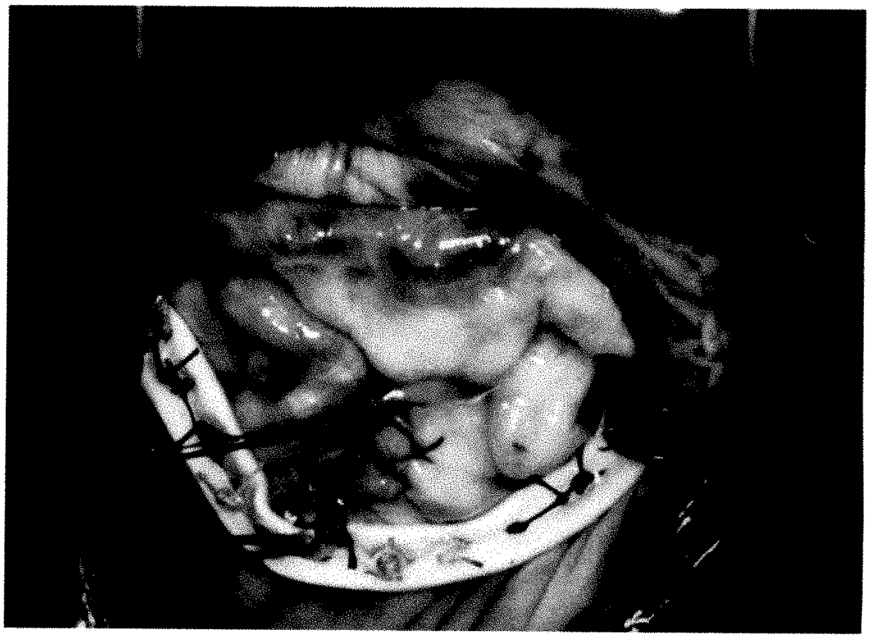

Fig 1. Posterior mitral annuloplasty with polytetrafluoroethylene prosthesis. Mattress sutures have been used to secure the prosthesis to the posterior annulus. Quadrangular resection and repair of the mural leaflet has been performed.

advantages. (1) It is effective (Table 1) and provides durable results (5% reoperation rate) comparable with those of other series [4]. (2) The PTFE prosthesis is a higly flexible device that conforms to the natural annulus, and it is strong enough to prevent future annular dilatation (no patient exhibited a clinically significant increase in mitral valve area in follow-up). (3) Plication or reduction of the posterior annulus can be tailored to every pathological finding with regard to either the site (central or commissural) or the entity. (4) It preserves a satisfactory valve orifice (similar to the one reported by David and co-workers [1]), and the transmitral flow indexes seem to show a nearly physiological flow (Table 1). (5) It does not lead to left ventricular outflow tract obstruction, sometimes observed with Carpentier's ring [5], avoiding systolic anterior motion of the aortic leaflet.

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Reply

To the Editor:

Doctor Fundaro and associates are to be congratulated on their innovative approach to mitral annuloplasty. We have employed a similar technique during the last 2 years in 100 cases with excellent results, but have found that this technique failed to meet one of the criteria that I enumerated in my discussion of the paper by David and associates. This type of approach does not result in a *measured* plication of the posterior annulus. Rather, the plication of the posterior annulus varies depending on the tension that the surgeon places on individual mattress sutures. If excessive tension is placed on the sutures, the posterior annulus can be reduced to the point where the posterior leaflet is virtually obliterated. A device to eliminate this problem is currently under investigation in the animal laboratory with promising results.

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Elevated Hemidiaphragm After Cardiac Operations

To the Editor:

The recent article by Curtis and associates [1] is similar to the data reported by us 2 years ago [2]. The article by Curtis and associates lists 20 references between 1957 and 1985, but for unknown reasons, it does not cite our publication. The conclusions are identical, namely that ice saline slush in the pericardium clearly is associated with a high frequency of phrenic nerve injury.

Our data showed a much higher frequency of diaphragmatic palsy (73%), probably reflecting a difference in intensity and duration of contact of the ice slush with the phrenic nerve. In our patients, the nerve injury was clinically significant, for 14% had serious respiratory disability. The report by Curtis and associates did not record an increase in morbidity, though one fatality was associated with bilateral phrenic injury.

Importantly, the data in the report by Curtis and associates does demonstrate the reversibility of hypothermic phrenic injury, as 97% of their patients had normal chest roentgenograms after 2 years of follow-up, a point that is important in this medicolegal age.

A number of reports have now clearly documented a high frequency of phrenic nerve injury with ice saline slush. Furthermore, to our knowledge, there are no data demonstrating enhanced myocardial preservation with slush that cannot be attained with cold saline solution. For this reason, we stopped the use of slush in all open heart procedures over 2 years ago.

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1. Curtis JJ, Nawarawong W, Walls JT, et al. Elevated hemidiaphragm after cardiac operations: incidence, prognosis, and relationship to the use of topical ice slush. Ann Thorac Surg 1989;48:764–8.
2. Esposito RA, Spencer FC. The effect of pericardial insulation on hypothermic phrenic nerve injury during open heart surgery. Ann Thorac Surg 1987;43:303–8.

Reply

To the Editor:

I appreciate being reminded of the important paper by Drs Esposito and Spencer [1]. The data collection and manuscript preparation for our report [2], although not published in final form until 1989, were completed in 1987, explaining our failure to cite their work.

Their paper is extremely important because it shows convincingly that the "liberal instillation of ice saline slush into the pericardial well every twenty minutes" will result in a high incidence of elevated diaphragm with attendant serious morbidity and mortality. Indeed it is difficult to understand why, in their prospective study, when elevated diaphragm developed in 3 of 4 consecutive patients, the practice was continued through 70 patients.

As the hazards of topical ice for myocardial cooling were well known, we tried to "get away" with the *single* application of ice slush to aid in rapid myocardial cooling. The slush was of melting snow consistency and was usually absent from the pericardial well ten minutes after application. In spite of this, we observed nearly a one in four incidence of elevated diaphragm. As we had only recently reintroduced the internal mammary artery as a conduit in our practice and the elevated diaphragm was almost always on the left, we felt that we were somehow damaging the phrenic nerve in the internal mammary artery preparation process. This proved not to be the case. We did show that when topical ice slush is used even for brief periods of time, the incidence of elevated diaphragm is greater when the internal mammary artery is harvested. Presumably this is because of greater proximity of the ice to the phrenic nerve. This is consistent with recent experimental findings by Robicsek and colleagues [3].

It seems clear that whether topical ice slush is administered briefly as in our report or liberally as in the report by Esposito and Spencer, the price to be paid for any salutatory benefit of this method of myocardial cooling will be an increased observation of elevated diaphragm with potentially serious consequences.

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References

1. Esposito RA, Spencer FC. The effect of pericardial insulation on hypothermic phrenic nerve injury during open heart surgery. Ann Thorac Surg 1987;43:303–8.
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Management of Jehovah's Witness Patients

To the Editor:

We have recently pretreated 3 members of the Jehovah's Witness sect with the synthetic erythropoietin marketed by Amgen Inc under the trade name of Epogen. All of these were elderly patients who were anemic and required a cardiovascular surgical procedure. Two required coronary artery bypass and 1, resection of an abdominal aneurysm. Pretreatment with Epogen stimulated the bone marrow as evidenced by an increase in the reticulocyte count and a rising hemoglobin level. Treatment was carried through into the postoperative period until the hemoglobin level returned to nearly normal.

We believe this is a safe and useful adjunct in dealing with patients of the Jehovah's Witness sect who require an operation in which blood loss and shortened red cell half-life can result in profound postoperative anemia. We recommend it as a safe and useful adjunct.

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PROGRAM

1990 INTERIM MEETING
THE SOCIETY OF THORACIC SURGEONS

September 21–23, 1990
Hyatt Regency Chicago, Chicago, Illinois

Friday, September 21, 1990

1:00 **Welcoming Remarks**
W. Gerald Rainer, President

Introduction to Program
Richard P. Anderson, Secretary and Interim Meeting Program Chairman

1:10–2:45 **Medico-Legal Session**
Moderator: Thomas D. Bartley, Chairman, Committee on Medico-Legal Affairs

STS Professional Liability Survey
Thomas D. Bartley

The AMA/Specialty Society Medical Liability Project
James S. Todd
Acting Executive Vice President, American Medical Association

California Tort Reform
Winfield J. Wells
Member, Committee on Medico-Legal Affairs

A Trial Lawyer's Perspective
Joseph D. Jamail
From the firm of Jamail and Kolius, Houston, TX

INTERMISSION

3:30–5:00 **Health Care in America**
Moderator: Richard P. Anderson

Health Care Needs—The Consumer Viewpoint
Robert E. McGarrah, Jr
Director for Public Policy, American Federation of State, County, and Municipal Employees

Health Care—A Political Perspective
The Honorable Richard D. Lamm
Professor, Leo Block Chair, Director, Center for Public Policy and Contemporary Issues, The University of Denver; Governor of Colorado, 1975–1987

The Health Care Industry
Austin Ross
Vice President and Executive Administrator, Virginia Mason Medical Center; Clinical Professor, University of Washington School of Public Health and Community Medicine; Chairman, Ad Hoc Committee on Physician Involvement, American Hospital Association; Consultant, W.K. Kellogg Foundation

Saturday, September 22, 1990

7:00–11:00 Two workshops will address reimbursement and coding.

7:00–8:30 **Physician's Breakfast Session**
This session will feature a representative from HCFA discussing recent changes affecting cardiothoracic reimbursement.

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9:00–11:30 **Coding Workshop for Office Personnel** (Physicians welcome)
Experts on CPT-4 and ICD-9 will explain the two coding systems and answer questions related to cardiothoracic billing.

8:30–9:45 **Plenary Session**
Moderator: W. Gerald Rainer

The Canadian Experience
Hugh E. Scully
Member, Committee on Physician Reimbursement

Thoracic Surgery Initiatives
George E. Miller, Jr
Chairman, Committee on Physician Reimbursement

INTERMISSION

10:30–12:00 **Plenary Session**

Paul B. Ginsburg
Executive Director, Physician Payment Review Commission
Washington, DC

Monica Noether
Senior Economist, Abt Associates, Inc
Cambridge, Massachusetts

Glenn R. Markus
STS Consultant on Physician Reimbursement and Government Relations
Health Policy Alternatives, Inc
Washington, DC

12:00–1:30 Luncheon
The Honorable Louis W. Sullivan
Secretary, Department of Health and Human Services

AFTERNOON SCIENTIFIC PROGRAM

2:00–5:45 **THREE PARALLEL SCIENTIFIC SESSIONS**

General Thoracic Surgery

2:00 Management of Stage IIIA Lung Cancer
Robert J. Ginsberg, New York, NY

2:20 Management of Barrett's Esophagus
F. Henry Ellis, Jr, Burlington, MA

2:40 Esophageal Diverticula
Mark B. Orringer, Ann Arbor, MI

3:00 Pulmonary Resection for Metastatic Disease
Thomas R. J. Todd, Toronto, Ont, Canada

INTERMISSION

4:10 Multimodality Treatment of Cancer of the Esophagus
Joseph I. Miller, Atlanta, GA

4:30 Mesothelioma
Nael Martini, New York, NY

Parallel Scientific Sessions, continued

4:50 Pancoast Tumor
Harold C. Urschel, Jr, Dallas, TX

5:10 Management of Achalasia
Mark K. Ferguson, Chicago, IL

Adult Cardiac Surgery

2:00 Challenges for Cardiac Transplantation in the Nineties
Bartley P. Griffith, Pittsburgh, PA

2:20 Heart-Lung Transplantation—1990
Bruce A. Reitz, Baltimore, MD

2:40 Current Status of Mechanical Circulatory Support
D. Glenn Pennington, St. Louis, MO

3:00 Cardiac Arrhythmia Surgery: Current Status and Future Directions
James L. Cox, St. Louis, MO

INTERMISSION

4:10 Surgery for Congenital Heart Disease in Adults
James K. Kirklin, Birmingham, AL

Valve Selection for Valve Replacement

4:30 Mechanical Valves
Cary W. Akins, Boston, MA

4:50 Bioprosthetic Valves
William R. E. Jamieson, Vancouver, BC, Canada

5:10 Homograft Valves
Robert B. Karp, Chicago, IL

5:30–5:45 Panel Discussion: Questions and Answers

Pediatric Cardiac Surgery

2:00 Fontan Procedure: Techniques and Results With Tricuspid Atresia and Complex Single Ventricle
Gordon K. Danielson, Rochester, MN

2:20 The Arterial Switch Operation for Simple and Complex Forms of Transposition
Edward L. Bove, Ann Arbor, MI

2:40 Surgical Management and Results in Infants with Pulmonary Atresia With Intact Ventricular Septum
William G. Williams, Toronto, Ont, Canada

3:00 Surgical Management of Coarctation in Infants and Children
Ralph D. Siewers, Pittsburgh, PA

INTERMISSION

4:10 Aortic, Mitral, and Pulmonary Valve Repair in Infants and Children
Aldo R. Castaneda, Boston, MA

4:30 Repair of Truncus Arteriosus in Infants
Kevin Turley, San Francisco, CA

4:50 Surgical Management of Tetralogy of Fallot
Vaughn A. Starnes, Stanford, CA

5:10 Anomalous Origin of the Left Coronary Artery From the Pulmonary Artery
John W. Brown, Indianapolis, IN

Sunday, September 23, 1990

7:00–10:30 **The Premier Presentation of the STS National Database**

7:00–8:00 **Introductory Session for Members and Guests**
A review of the evolution and development of the National Database with a presentation of the first 50,000 cases.

8:30–10:30 **Solving a Problem—Serving a Need**
A live demonstration of the National Database featuring a walk-through of the data entry forms, risk stratification system, data screens, and report capabilities with a focus on how the National Database can assist a cardiothoracic surgeon in his or her practice.

8:00–10:00 **PLENARY SESSION**

8:00 **Lung Transplantation**
Joel D. Cooper, St. Louis, MO

8:40 **Hypoplastic Left Heart Syndrome**
Moderator: Aldo R. Castaneda, Boston, MA

Surgical Repair
William I. Norwood, Jr, Philadelphia, PA

Cardiac Transplantation
Constantine Mavroudis, Chicago, IL

9:20 **Coronary Revascularization**

Angioplasty—Current Indications and Results
Spencer B. King, Atlanta, GA

Coronary Bypass—Current Indications and Results
Floyd D. Loop, Cleveland, OH

10:45–12:00 **THREE PARALLEL HOW-TO-DO-IT SESSIONS**
General Thoracic Surgery

10:45 Management of Infected Median Sternotomy Wounds
Geoffrey M. Graeber, Morgantown, WV

11:00 Intrathoracic Lung Cancer Staging
G. Alexander Patterson, Toronto, Ont, Canada

11:15 Sleeve Lobectomy
L. Penfield Faber, Chicago, IL

11:30 Ivor-Lewis Esophagogastrectomy
Victor F. Trastek, Rochester, MN

11:45 Postpneumonectomy Empyema
Peter C. Pairolero, Rochester, MN

Adult Cardiac Surgery

10:45 Revascularization With the Gastroepiploic Artery
Bruce W. Lytle, Cleveland, OH

11:00 Retrograde Cardioplegia
W. Randolph Chitwood, Jr, Greenville, NC

11:15 Adult Homograft Aortic Valve Replacement: Surgical Challenges Requiring a Spectrum of Techniques for Solution
Richard A. Hopkins, Washington, DC

11:30 Mitral Valve Repair—1990
Delos M. Cosgrove III, Cleveland, OH

11:45 Treatment of Aortic Dissection—Updated
E. Stanley Crawford, Houston, TX

Parallel How-to-Do-It Sessions, continued

Pediatric Cardiac Surgery

10:45	Postoperative Management of Pulmonary Hypertension in Infants and Children Including ECMO James A. Alexander, Gainesville, FL
11:00	Atrioventricular Septal Defect Repair in Infancy Frank M. Midgley, Washington, DC
11:15	What to Do If It Can't Be Fixed: Closed Palliative Procedures Anthony L. Moulton, Omaha, NE
11:30	Surgical Ablation of Arrhythmias in Children David A. Ott, Houston, TX
11:45	Cryopreserved Allograft Valve Conduits and Vascular Tissue in the Repair of Complex Congenital Heart Disease David R. Clarke, Denver, CO
12:00	ADJOURNMENT

GENERAL INFORMATION

Registration and Fees

An advance registration form with hotel reservation information will be mailed to Society members. Nonmembers should write to the Secretary, Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

Members and Candidate Members are not required to pay a registration fee for the general sessions. The fee for other physicians is $200, except guest speakers. Each resident will be charged $30 and will be required to present a letter from his or her chief of service to take advantage of this discounted fee. This letter can accompany an advance registration form or be presented at the time of on-site registration. If no letter accompanies the registration form, he or she will be charged the guest fee of $200. Nurses and paramedical personnel may register upon payment of a $30 registration fee and presentation of a letter of introduction from a Society member.

Accreditation

The Interim Meeting of The Society of Thoracic Surgeons is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. One credit hour in Category I of the Physician's Recognition Award of the American Medical Association may be claimed for each hour of participation by the individual physician.

1991 Annual Meeting of The Society of Thoracic Surgeons

The 1990 meeting is an Interim Meeting to be held at the Hyatt Regency Chicago in Chicago, Illinois, September 21–23, 1990. No abstracts are solicited for that program.

The Twenty-seventh Annual Meeting will be held at the San Francisco Moscone Center in San Francisco, California, February 18–20, 1991.

APPLICATION FOR MEMBERSHIP

(Deadline: September 1, 1990)

Requests for application forms for membership in The Society of Thoracic Surgeons should be addressed to James L. Cox, MD, Chairman, Membership Committee, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

The completed application forms and supporting letters must be in the hands of the Membership Committee by **September 1, 1990,** for the applicant to be considered for election at the meeting in February 1991.

CALL FOR ABSTRACTS

(Deadline: September 12, 1990)

Abstracts for papers to be presented at the 1991 Annual Meeting are now being accepted. The deadline for receipt of abstracts is September 12, 1990. An original and one copy should be submitted, using the official Society abstract form (on verso of this page), to Alexander S. Geha, MD, and Robert A. Guyton, MD, Co-Chairmen, Program Committee (Abstracts), The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601. Additional forms are available upon request from The Society. Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. Abstracts must be in the hands of the Program Committee by **September 12, 1990.** Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

The Thoracic Surgery Directors Association (TSDA) has established a Resident Presentation Award for 1991. Potential TSDA Resident Award abstracts must represent original work by the resident, who is to be first author and presenter. TSDA Resident Award abstracts may be directed to the regular Scientific Session or the Research Forum.

Essayists are reminded that according to the bylaws of The Society, all papers accepted for presentation: (1) must be submitted in *triplicate* to the Secretary at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation; and (2) become the property of The Society if they are accepted for presentation.

It is well recognized that abstracts frequently belie their content by virtue of poor organization, and as a result valuable contributions to the Scientific Sessions may be unrecognized. It is important that methods and results be clearly defined in the abstract; therefore, general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Speakers for accepted papers are limited to ten minutes.

Instructions for Abstracts

The official abstract form printed on verso of this page and available from The Society, or photocopies thereof, must be used. **Authors must categorize the principal subject of their abstract by checking the appropriate box.**

If the author wishes to submit the abstract for consideration for the Thoracic Surgery Directors Association Award competition, the *additional* appropriate box must be checked. Also, the name of the Program Director must appear on a TSDA Resident Award abstract.

1. Full names of authors must appear on the abstract.
2. Institution or address is to be given, but omit titles, degrees, and appointments.
3. Abstracts must be limited to 250 words and must be typed double-spaced.
4. When percentages are used, the absolute numbers of derivation must be stated.
5. The body of the abstract should include:
   a. A brief statement of the purpose of the study being presented, with reference to the current state of research in the field.
   b. The methods of study or experimental approach clearly, but briefly, defined.
   c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
   d. A statement concerning the significance of the work and its possible implications for further research.
6. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

In discussion of papers, The Society encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of discussion in the form of "secondary papers" will not be welcomed.

CALL FOR SURGICAL FILMS OR VIDEO TAPES

(Deadline: September 1, 1990)

The popular surgical movie program will again be presented at the San Francisco meeting. The Program Committee hereby solicits the submission of surgical films, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to The Society. The film may not exceed ten minutes in length. Sound movies are acceptable but not necessary; however, live narration by the principal surgeon is a requirement for participation in the movie night program. The movies should be on 16-mm film or ¾-inch U-Matic video tape. The deadline for submission is **September 1, 1990.** Films and video tapes also should be sent to Alexander S. Geha, MD, and Robert A. Guyton, MD, Co-Chairmen, Program Committee, at The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

Richard P. Anderson, MD
Secretary

For Committee use only:

THE SOCIETY OF THORACIC SURGEONS

Abstract Form

For Committee use only:
Rating: (Highest 1)

1☐ 2☐ 3☐ 4☐ 5☐

LIMIT TO 250 WORDS AND DOUBLE-SPACE

TITLE
AUTHOR(S)
ADDRESS

PLEASE CHECK ONE APPROPRIATE CATEGORY

- ☐ Pulmonary
- ☐ Esophagus
- ☐ Chest wall Mediastinum
- ☐ Trauma
- ☐ Transplantation
- ☐ Heart
- ☐ Great vessels
- ☐ Valves
- ☐ Congenital
- ☐ Coronary
- ☐ Electrophysiology
- ☐ Myocardial protection
- ☐ Extracorporeal circulation
- ☐ Endoscopy
- ☐ Vascular surgery
- ☐ Research, Cardiac
- ☐ Research, Congenital Cardiac
- ☐ Research, Transplantation
- ☐ Research, General Thoracic

☐ **PLEASE CHECK IF ALSO SUBMITTED FOR THE THORACIC SURGERY DIRECTORS ASSOCIATION AWARD**

Program Director's Name:

I acknowledge that the material will not be presented elsewhere if accepted for presentation on The Society of Thoracic Surgeons Scientific Program. I further understand that the Editorial Board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

Signature of Senior Author

Information About Membership in The Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) is the largest organization of its kind devoted primarily to the practice of thoracic and cardiovascular surgery. The major purpose of The Society is educational, with the aim of providing thoracic and cardiovascular surgeons from both academic and private practice environments a forum for presentation and discussion of scientific topics. As outlined in the original bylaws of The Society, this educational emphasis is designed to accomplish the broader goal of improving the quality and practice of thoracic and cardiovascular surgery as a specialty.

The STS recently celebrated its 25th Anniversary, having been founded in 1964. Since its inception, The Society has grown continually so that at present the membership includes the majority of board certified thoracic surgeons in the United States as well as thoracic and cardiovascular surgeons from 45 other countries.

In addition to an annual scientific meeting, the STS has more than 20 committees working on diverse matters related to improving thoracic and cardiovascular surgery as a specialty. Examples of these committees are: Standards and Ethics, Government Relations, Medico-Legal Affairs, Surgical Standby for PTCA, Physician Reimbursement, CPT-4 Advisory, Education and Resources, and Cardiothoracic Surgical Practice Guidelines. The Committee to Analyze Circulatory Assist Devices and Artificial Hearts sponsors topical meetings (next meeting, November 15–17, 1991, in San Francisco). The Committee to Develop a National Database for Thoracic Surgery plans to implement the first comprehensive database program for thoracic and cardiovascular surgeons in the United States; it will be offered to members in the near future.

There are five types of membership in The Society of Thoracic Surgeons: active, senior, honorary, international, and candidate.

Active Member Applicants for active membership must be surgeons whose practice is devoted primarily to the field of thoracic and cardiovascular surgery.

QUALIFICATIONS: Applicants must be Diplomates of the American Board of Thoracic Surgery or Fellows in The Royal College of Surgeons of Canada, and be established in the practice of thoracic and/or cardiovascular surgery for a minimum of three years. There must be sponsoring letters from three active STS members.

Senior Member Any active member or international member, upon reaching the age of sixty-five years, shall automatically become a Senior Member.

Honorary Member Honorary Membership shall be reserved for distinguished persons worldwide who have achieved prominence in the field of thoracic and cardiovascular surgery and have contributed to its advancement. Honorary members shall be elected by a majority vote of The Society at its annual business session upon recommendation of the Council of the STS.

International Member Members from countries other than the United States and Canada were previously accepted only as active members. Because of differences in training and practice, the application process for foreign members was often complex and time consuming. To allow for greater participation by thoracic and cardiovascular surgeons from other countries, the bylaws have been revised to provide for a category of International Member, which is the category for all members outside the United States and Canada.

QUALIFICATIONS: Applicants shall reside outside the United States and Canada. Their training in this specialty shall be considered equivalent to that of Active Members. They shall have achieved appropriate certification or recognition of achievements in this specialty in their country and must devote the majority of their professional efforts to the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee.

Candidate Member Candidate membership was created to allow participation of younger surgeons in the time prior to being qualified for active membership.

QUALIFICATIONS: Applicants shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a similar program approved for training by The Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in process of acquiring certification by the American Board of Thoracic Surgery or The Royal College of Surgeons of Canada are eligible for this type of membership.

If you would like to receive an application for membership in The Society, send the request printed below. This year's deadline for receipt of applications is September 1, 1990. We suggest you apply soon as it takes time to process the application. Approved applications will be presented to the membership at the February 1991 Annual Meeting in San Francisco.

REQUEST FOR APPLICATIONS

Please send an application for: ☐ Active membership ☐ International membership ☐ Candidate membership

TO: NAME: ____________________

ADDRESS: ____________________

____

TELEPHONE NUMBER: ____________________

Send to: James L. Cox, MD, Chairman, Membership Committee
The Society of Thoracic Surgeons, 111 East Wacker Drive, Suite 600, Chicago, IL 60601
Telephone: (312) 644-6610; FAX: (312) 938-1214

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery,* 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

New Devices for the Cardiac and Peripheral Vascular Laboratories, Orlando, Florida—July 2–6, 1990

This meeting is sponsored by the Pittsburgh Vascular Institute and the Pittsburgh Heart Institute of Shadyside Hospital, Pittsburgh, PA, and is accredited for 15 hours in category 1 of the Physician's Recognition Award of the AMA. For information on this meeting, contact Shadyside Hospital, New Devices Technology Workshop, 5230 Centre Ave, Pittsburgh, PA 15232; or telephone (412) 622-1051.

Seventh Congress of the European Society of Biomechanics, Aarhus, Denmark—July 8–11, 1990

For information on this meeting, contact Seventh Congress of ESB, Biomechanics Laboratory, Orthopaedic Hospital, Randersvej 1, 8200 Aarhus N, Denmark; or telephone 45-616-7500, extension 4649.

Myocardial Preservation Into the 21st Century, Oxford, England—August 12–15, 1990

For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Drive, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870 (facsimile: (714) 759-6911).

Thirty-ninth Annual Meeting of the Scandanavian Association for Thoracic and Cardiovascular Surgery and the Scandanavian Society for Extracorporeal Technology, Reykjavík, Iceland—August 29–31, 1990

For information on this meeting, contact G. Ólafsson, MD, Chairman, Department of Thoracic and Cardiovascular Surgery, Landspítalinn, University Hospital, Reykjavík, Iceland.

Thirty-ninth Congress of the European Society for Cardiovascular Surgery, Budapest, Hungary—September 9–12, 1990

For information on this meeting, contact Budapest Convention Centre, H-1444, PO Box 233, Budapest XI, Jagello u 1-3, Hungary; or telephone (361) 852-507 (facsimile: (361) 665-636; telex: 22-7717).

Fourth Annual Meeting of the European Association for Cardio-thoracic Surgery, Naples, Italy—September 17–19, 1990

For information on this meeting, contact the Organizing Secretariat, MCM, Rione Sirignano, 5, 80121 Naples, Italy; or telephone (0)81/7611085-7611277 (facsimile: (0)81/664372; telex: 710626).

Second Annual Meeting of the International Society for Applied Cardiovascular Biology, Venice Lido, Italy—September 17–20, 1990

For information on this meeting, contact the Congress Secretariat, Kele Teo, San Marco 4930, Venice, Italy.

Interim Meeting of The Society of Thoracic Surgeons, Chicago, Illinois—September 21–23, 1990

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

Mechanical Circulatory Support 1990, London, England—September 26–28, 1990

For information on this meeting, contact Anne Sumner, Mechanical Circulatory Support 1990, Medical Research Services, 60 Oxford St, Southampton SO1 1DL, Hants, England; or telephone 0703 231068.

Controversies in Cardiovascular Disease: Surgical Versus Medical Treatment, Aalst, Belgium—September 28–29, 1990

For information on this meeting, contact Dr F. Wellens, Department of Cardiovascular Surgery, O.L. Vrouwziekenhuis, Moorselbaan 164, B-9300 Aalst, Belgium; or telephone 053/78 53 53 (facsimile: 053/78 38 76).

American College of Surgeons, San Francisco, California—October 7–12, 1990

For information on this meeting contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-sixth Annual Scientific Assembly, American College of Chest Physicians, Toronto, Ontario, Canada—October 22–26, 1990

This meeting is sponsored by the American College of Chest Physicians and the International Academy of Chest Physicians and Surgeons. For information, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association, Cerromar Beach, Puerto Rico—November 8–10, 1990

For information on this meeting, contact Gordon F. Murray, MD, Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610 (facsimile: (312) 938-1214).

Sixty-third Scientific Session of the American Heart Association, Dallas, Texas—November 12–15, 1990

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 750-5300.

Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons, San Francisco, California—February 17–20, 1991

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

CLASSIFIED ADS

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Media for Medicine, Inc, 440 Park Avenue South, New York, NY 10016 (telephone: (212) 684-5540; facsimile: (212) 545-0651). All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.10 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $15.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad orders should be for a maximum of 6 months; ads may be renewed for up to 6 months at a time. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3695). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the ad. To respond to an anonymous ad, write to Box Number, *The Annals of Thoracic Surgery*, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Cardiothoracic surgeon wanted for a busy, expanding, 3-man, private practice group in the Midwest. Applicant must be ABTS eligible or certified. Prefer recent graduate with some background in electrophysiologic surgery. Please send curriculum vitae.

Please respond to Box 189. 189H/G

Associate Director for Heart Transplantation is urgently needed for rapidly expanding heart transplantation program in California.

Please respond with curriculum vitae to the Pacific Cardiothoracic Surgery Group, 201 S Alvarado St, Suite 626, Los Angeles, CA 90057. 240L/K

Cardiovascular and thoracic surgeon, board eligible/certified, wanted to join well-established private practice located in Ft. Lauderdale, FL. Send CV.

Please respond to Box 251. 251L/K

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to Box 252. 252G/L

Cardiovascular and thoracic surgeon: Position available for board certified or board eligible person to join busy practice involved in adult cardiac, thoracic, and vascular surgery in major New England city. Association will lead to partnership. Excellent fringe benefits. Please send curriculum vitae.

Please respond to Box 291. 291B/G

Cardiothoracic/vascular surgeon wanted to join established practice in Ohio. Recent graduate preferred. Please submit curriculum vitae and three references.

Please respond to Box 302. 302C/I

Cardiac surgeon wanted to join established private practice in Eastern PA. Primarily adult cardiac. BC/BE required. Please send CV.

Please respond to Box 315. 315D/I

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another physician in private practice in Northeast. Immediate availability. Please respond with curriculum vitae.

Please respond to Box 316. 316D/I

Excellent opportunity for recent graduate, board eligible or certified, for private practice of cardiac, thoracic, and major vascular cases in Great Lakes area. Include references and curriculum vitae.

Please respond to Box 335. 335E/G

Cardiothoracic surgeon needed for expanding program in mid-Michigan. Primarily adult cardiac and thoracic. BC/BE required. Please send CV with references.

Please respond to Box 337. 337E/J

Cardiovascular and thoracic surgeon: Position available for a board certified or eligible cardiovascular and thoracic surgeon to join a 2-man private practice involved with adult cardiac, thoracic, and peripheral vascular surgery in a desirable eastern metropolitan area. Association features competitive salary, excellent fringe benefits, and a goal of early partnership. Please send curriculum vitae.

Please respond to Box 339. 339E/G

Cardiothoracic surgeon: Excellent opportunity in mid-West for experienced cardiothoracic surgeon to join highly regarded board-certified physician who is Chief of Cardiothoracic Service at 450-bed community teaching hospital. Very active practice in adult open hearts and general thoracic. Private practice association leading to partnership.

Please contact Jeanne Dowrick, Fulton, Longshore and Associates, 527 Plymouth Rd, Plymouth Meeting, PA 19462; telephone (800) 346-8397 or (215) 834-6780. 341E/G

Cardiothoracic surgeon wanted for busy, expanding Southeastern private group in regional medical center with university affiliation. Practice includes most aspects of adult and pediatric cardiac and thoracic surgery. Surgeon must be board eligible or certified with contemporary training. Excellent opportunity for suitable applicant.

Please respond to Box 342. 342F/I

Cardiothoracic surgeon: The Oregon Health Sciences University, Division of Cardiopulmonary Surgery, with strong active programs in all aspects of cardiopulmonary surgery and heart transplantation, has an academic position available at the Assistant Professor level. Candidates should be eligible for or certified by the American Board of Thoracic Surgery. Outstanding opportunity for an individual with excellent clinical skills, a track record of academic productivity, and a commitment to research and teaching. Two to four years of post-residency clinical experience is highly desirable.

Applicants are invited to respond with curriculum vitae to Adnan Cobanoglu, MD, Professor and Chief, Division of Cardiopulmonary Surgery, The Oregon Health Sciences University, 3181 SW Sam Jackson Park Rd, Portland, OR 97201. 346F/G

Thoracic surgery residency: Residency in thoracic surgery. Position available July 1991 at the University of Massachusetts Medical School/Hospital. Three-year program includes training in adult and pediatric cardiac and general thoracic surgery.

Interested candidates may contact Thomas J. Vander Salm, MD, Department of Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655. 347F/H

Cardiovascular and thoracic surgeon: Excellent opportunity to join a busy north central Florida group. Practice specializes in adult cardiac and thoracic surgery. Excellent benefit package. Please reply with curriculum vitae.

Please respond to Box 348. 348F/K

Cardiovascular and thoracic surgeon, BE/BC, to join in 2-man private practice in cardiovascular and thoracic surgery in the

Northeast. Excellent benefits package. Association will lead to partnership. Please send curriculum vitae.

Please reply to Box 350. 350F/K

Cardiovascular surgeon—to join two Diplomates of Thoracic Surgery in a practice located in east central Michigan. Group includes physician assistants, surgical technicians, registered nurses, and ancillary office personnel. Perfusionists are hospital based. The group has 2 months' elective wait list. Eighty percent of practice is coronary bypass.

Please respond to Box 351. 351G

Assistant surgeon sought for busy adult cardiothoracic surgery practice. Entire responsibility will be to assist 4 senior surgeons in the operating room. Board certification or eligibility in general surgery and some experience in vascular and/or thoracic surgery helpful, though not essential. Generous salary and fringes. Position is available immediately and could be permanent. Ideal location in very pleasant, small city near major eastern metropolitan centers.

Please respond to Lawrence I. Bonchek, MD, 555 North Duke St,
Lancaster, PA 17603; (717) 295-8395. 352G/H

Position available for thoracic boarded (or eligible) surgeon with large private group practice based in metro-NYC area (Newark). University affiliated (UMDNJ).

Please send CV to D. C. Syracuse, MD, 5 Franklin Ave, Suite 310,
Belleville, NJ 07109. 353G

Cardiothoracic surgeon needed for established program in scenic Montana. Unique opportunity for congenial private practice lifestyle combined with high-tech hospital environment including dedicated cardiac OR, cardiac anesthesia, and cardiac intensive care unit. Solo practice or association leading to partnership. Could be experienced surgeon or recent graduate from quality program.

Please respond to Box 354. 354G/L

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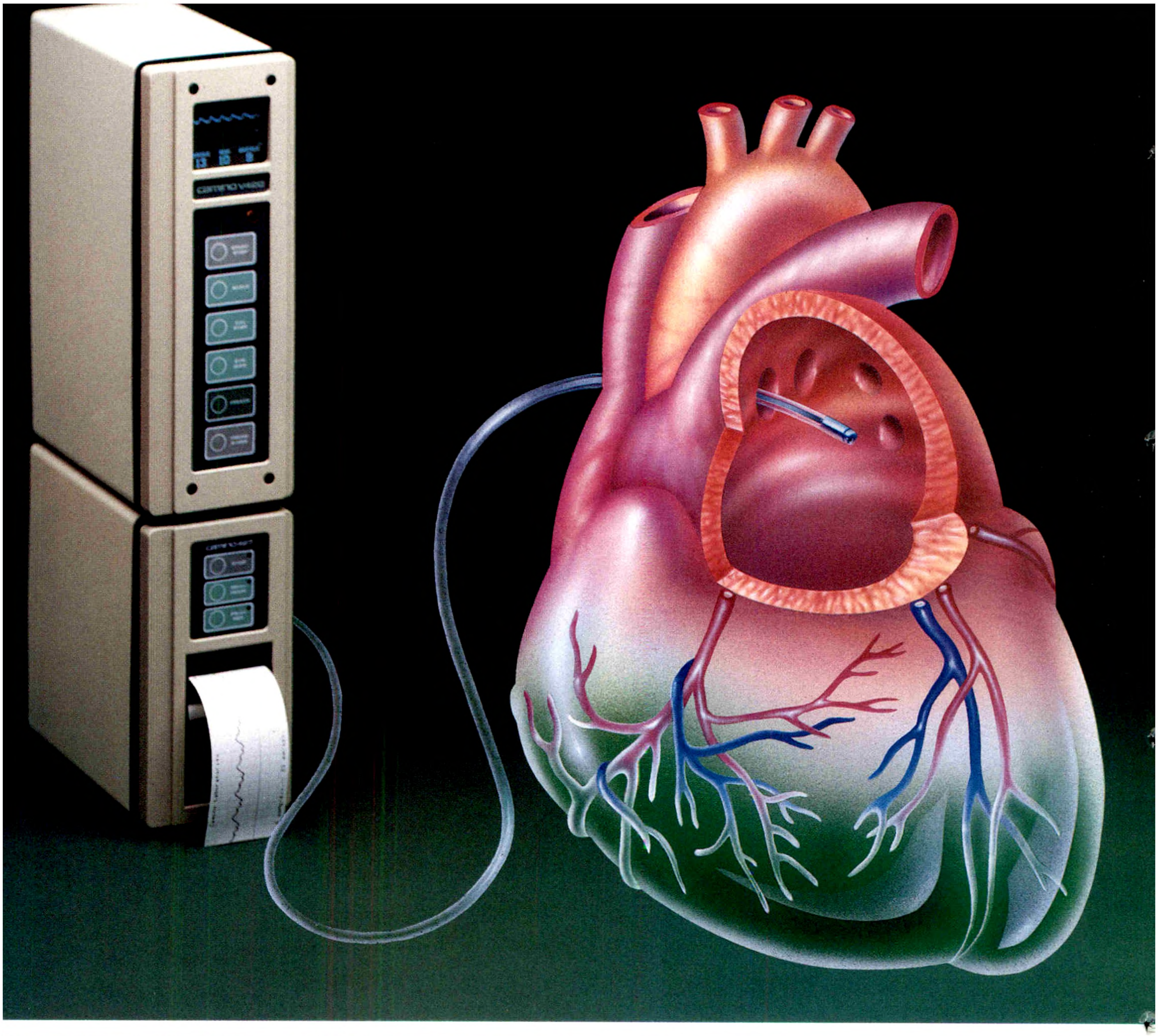

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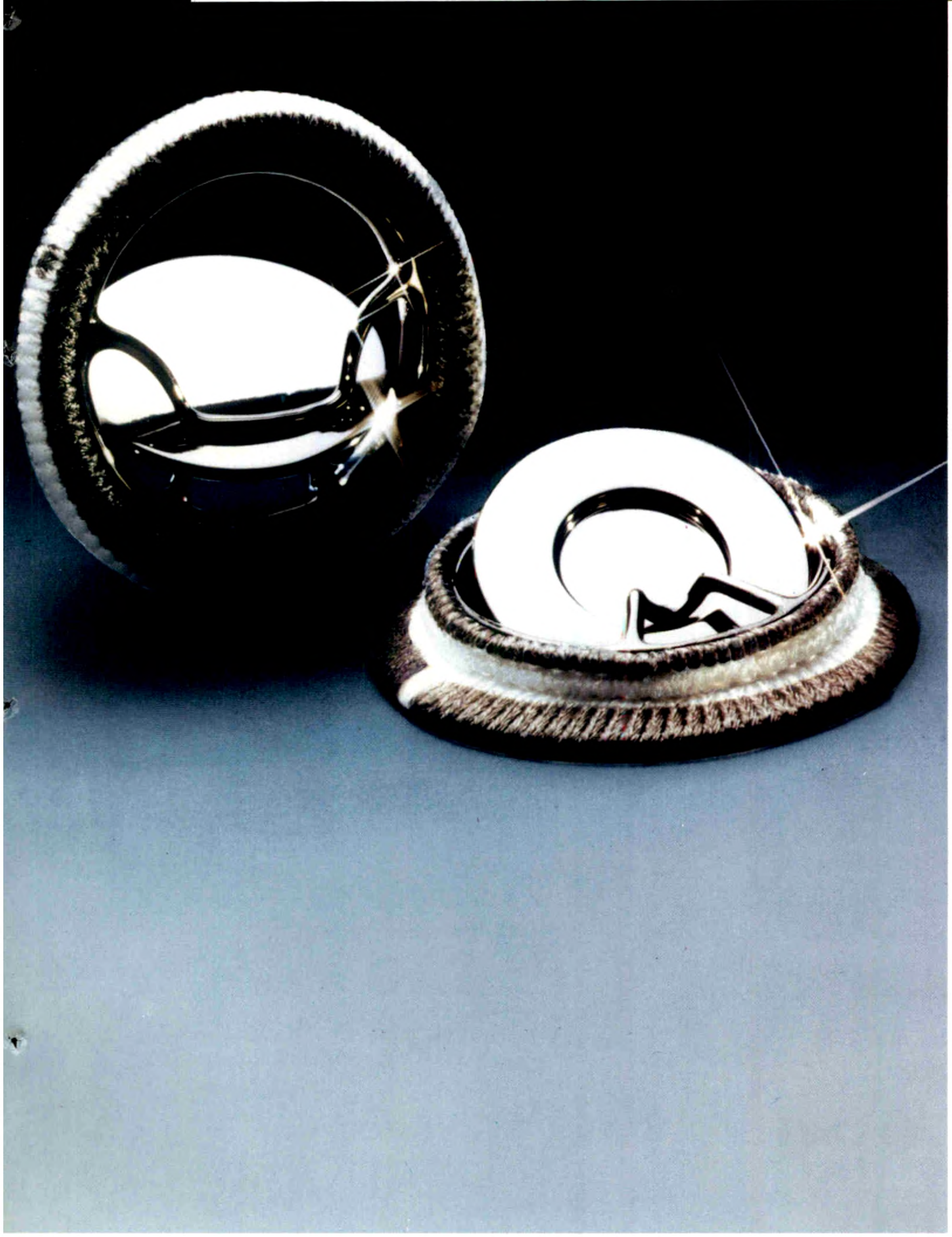

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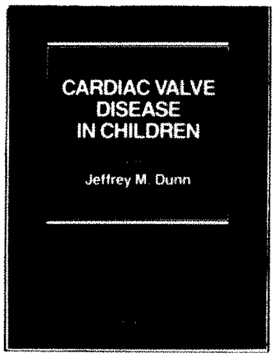

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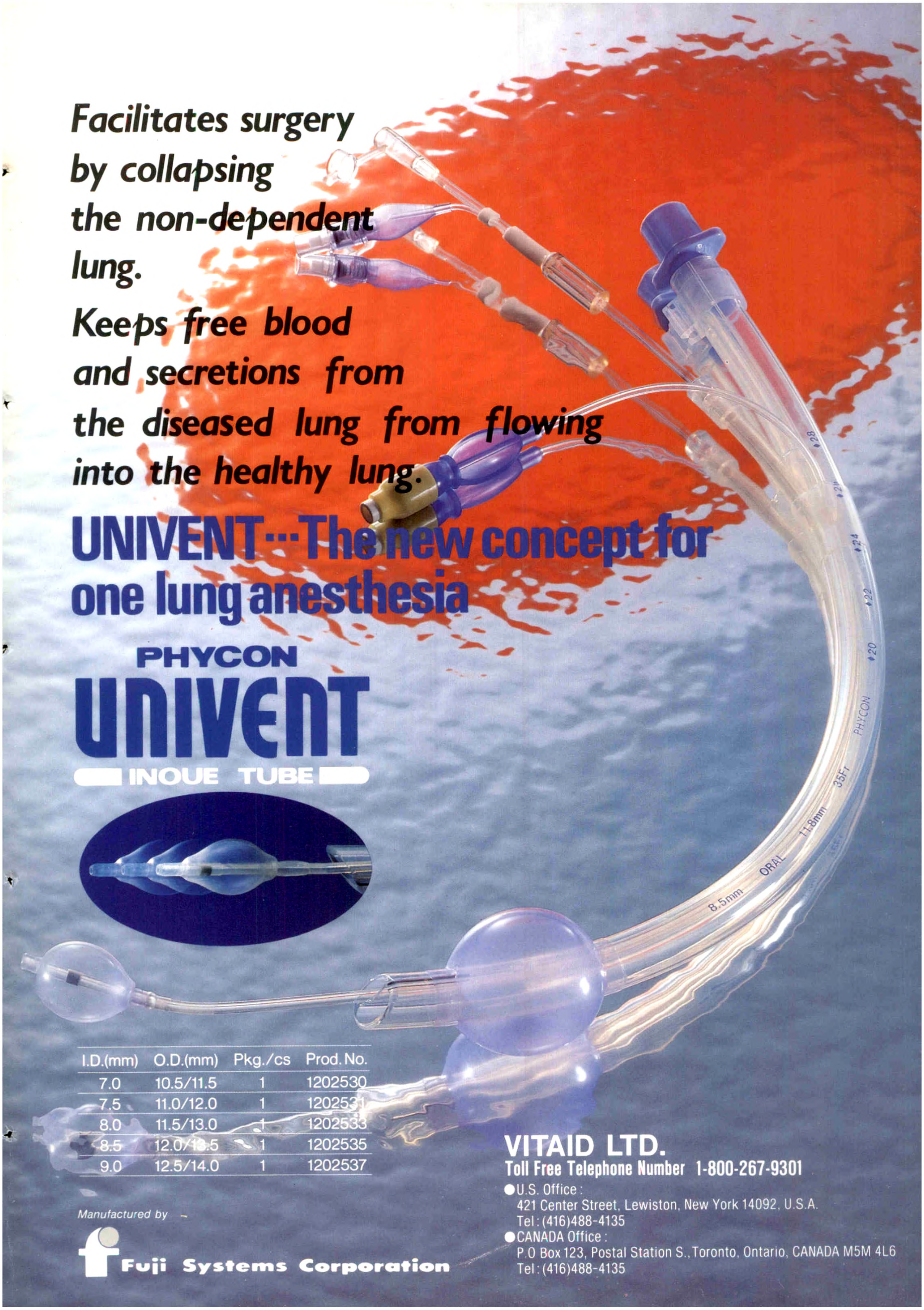

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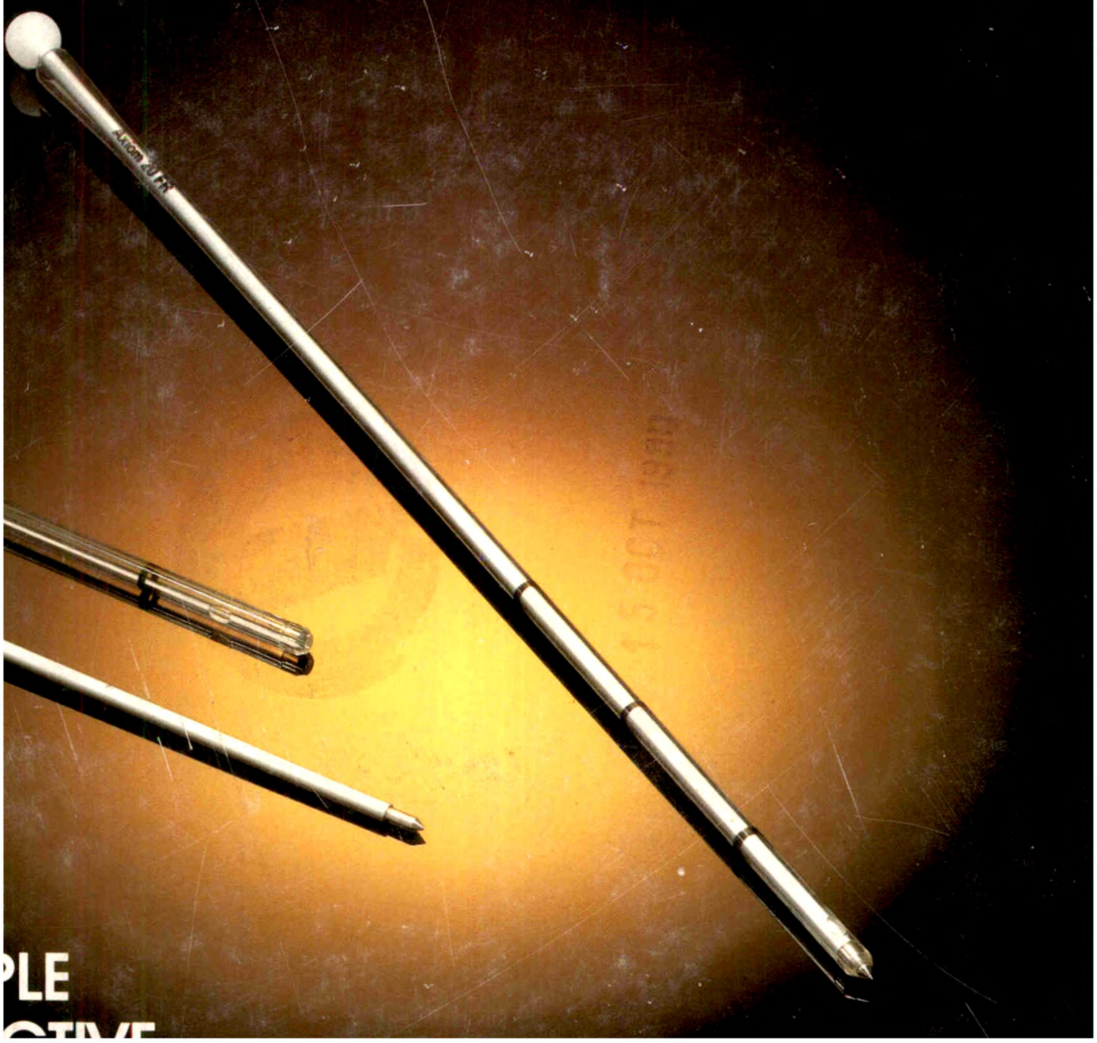

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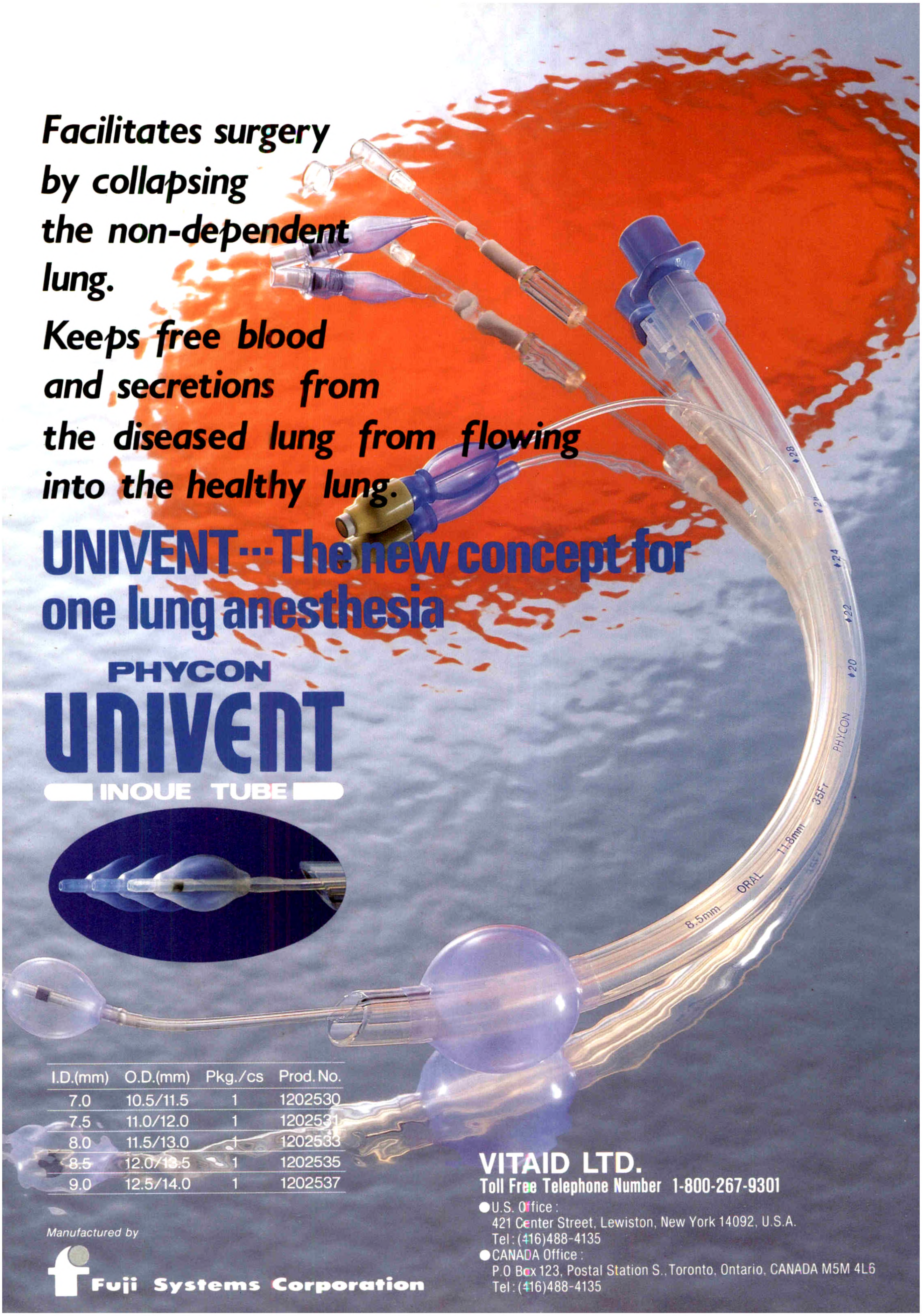

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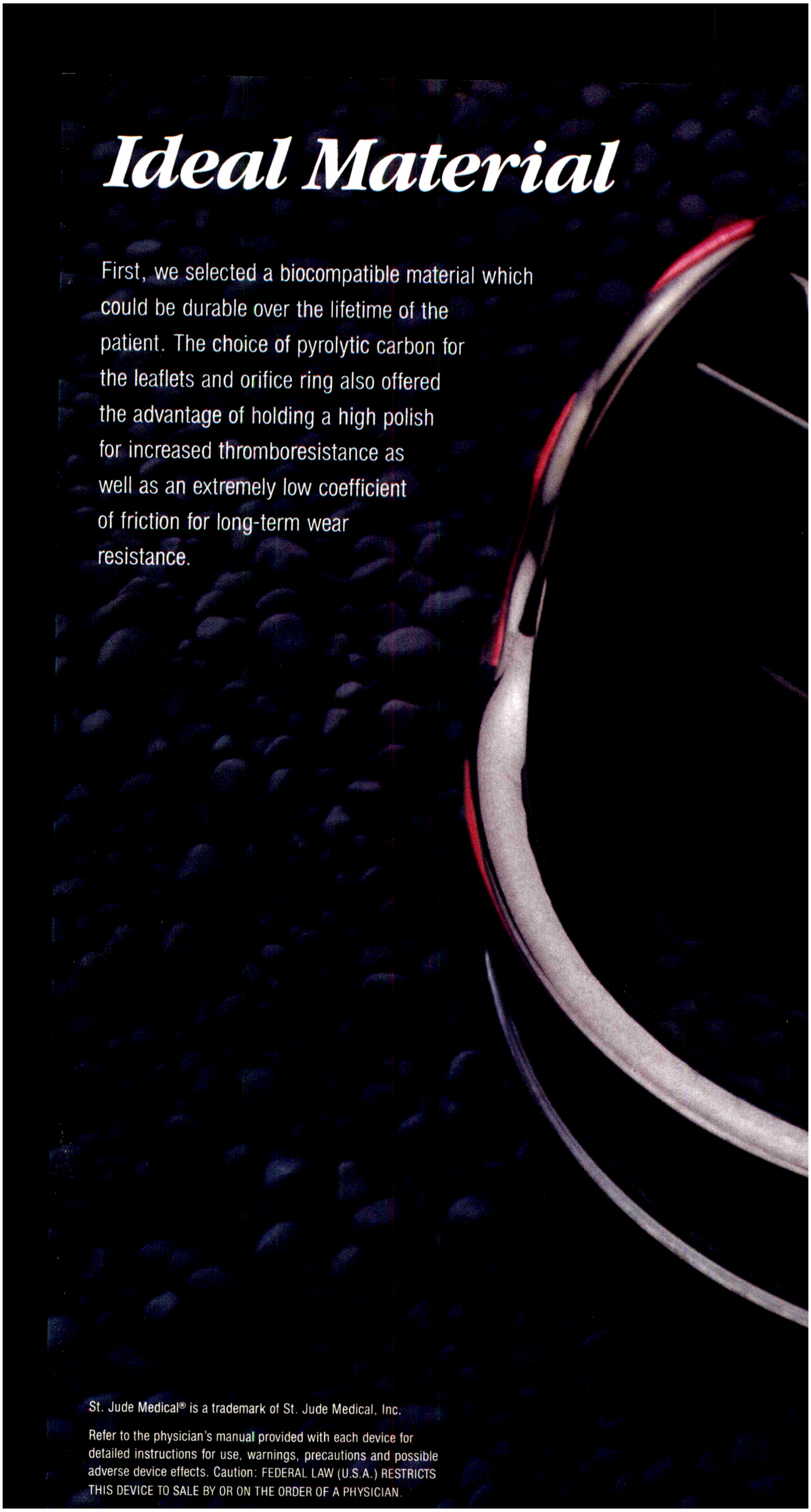

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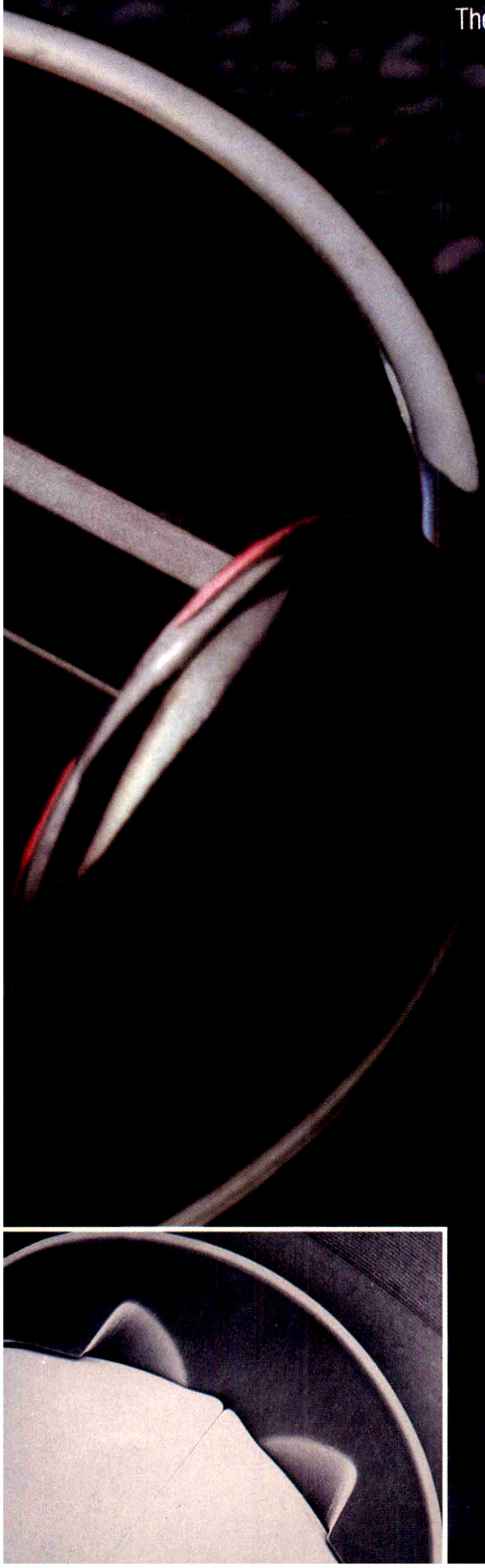

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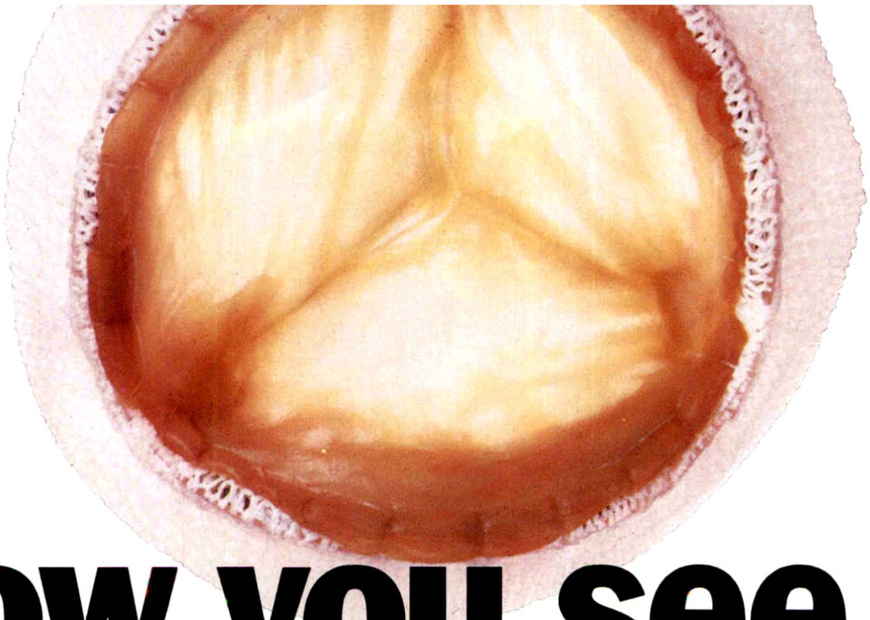

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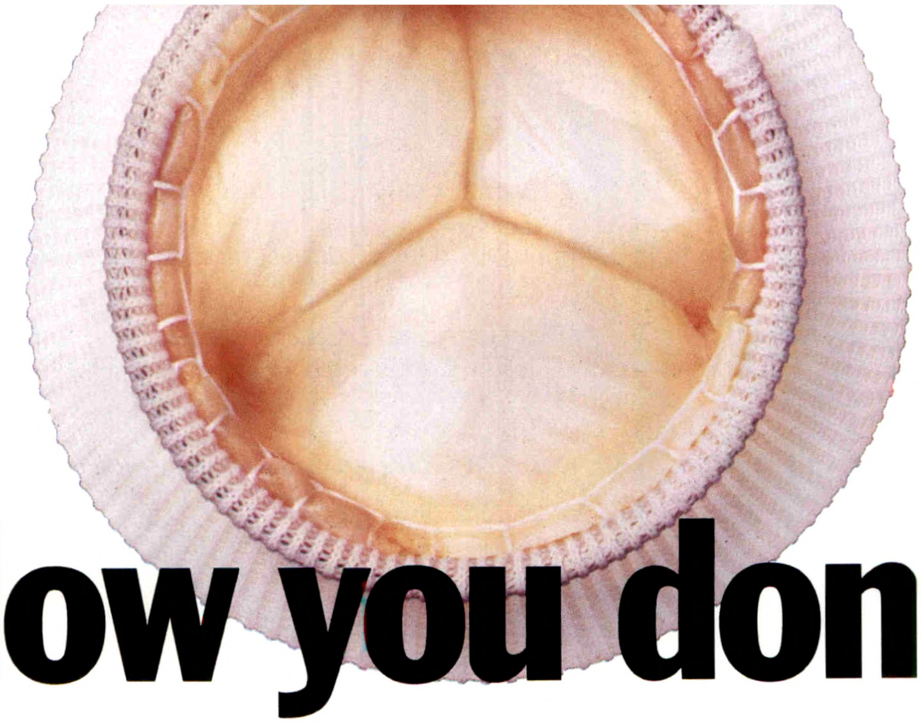

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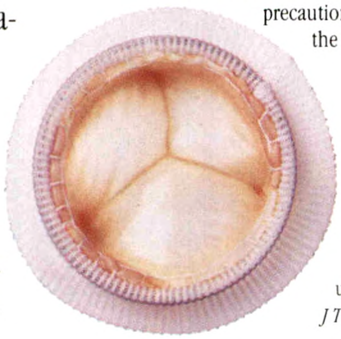

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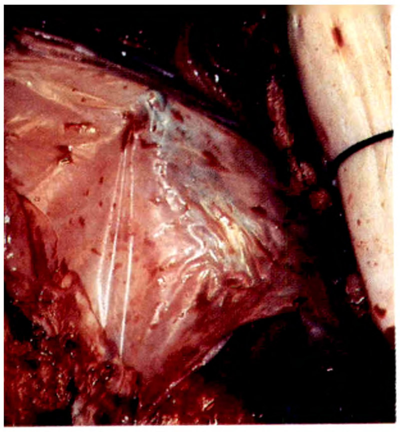

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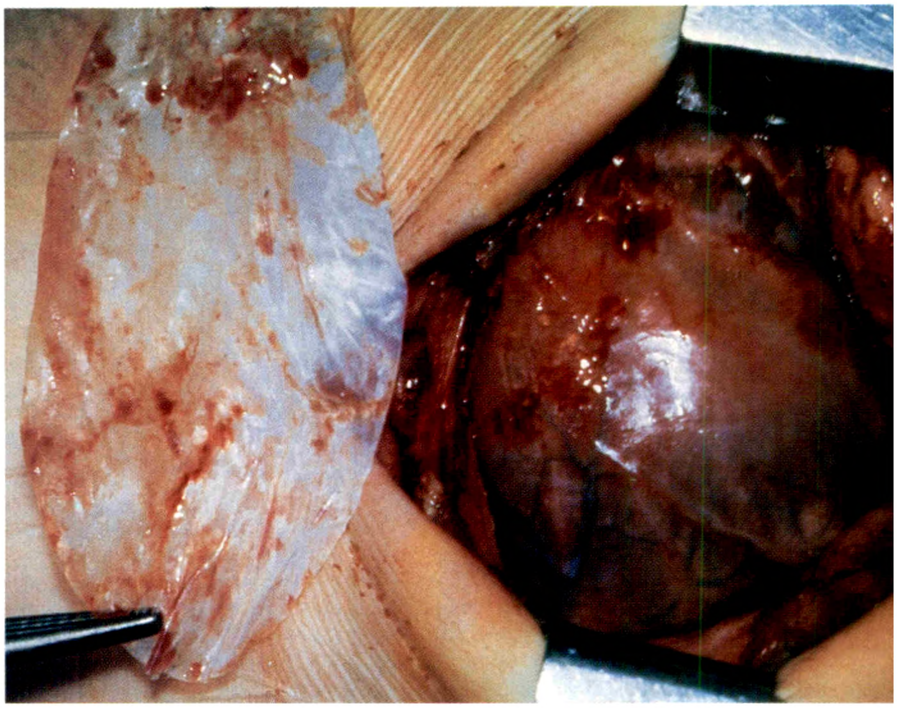

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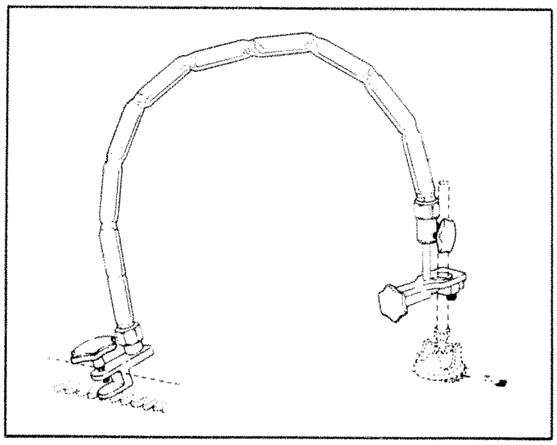

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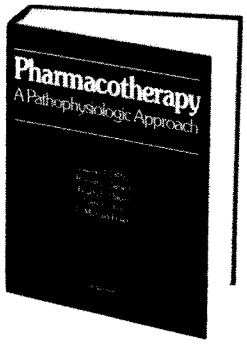

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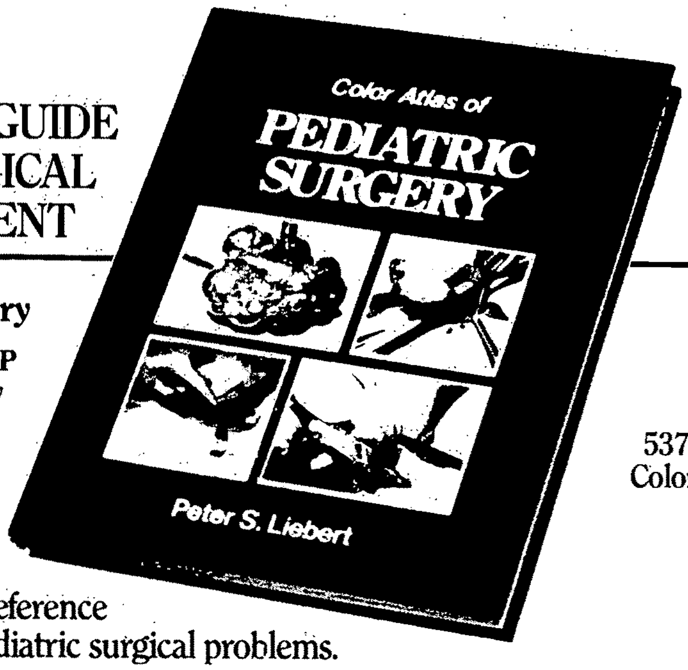

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Uncomfortable Issues

L. Henry Edmunds, Jr, MD

Division of Cardiothoracic Surgery, Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

Not many years ago, open heart operations for octogenarians were considered ill-advised if not reckless. However, technical progress and an aging population have changed perceptions; these operations, as represented by the report of Deleuze and colleagues [1], are now legitimate. Nevertheless, cardiac operations in aged and high-risk patients raise uncomfortable issues. Among these are risk assessment, patient selection, personal statistics, the right to an operation, and the obligations and responsibilities of surgeons who treat high-risk patients.

By virtue of age, octogenarians undergo open heart operation at "high risk," which does not need numerical definition for this essay. However, the term *octogenarians* describes a heterogeneous cohort of patients that differs from other patient groups by the single criterion of advanced age. Within the cohort of octogenarians there are low-, medium-, and high-risk patients as defined by specific descriptors (eg, malnutrition, emergency operation, New York Heart Association class IV) that have been identified as independent incremental risk factors for operative mortality and morbidity [2]. Knowledge of independent incremental risk factors for well-defined populations of patients permits estimates of the probability of death or serious morbidity for individual patients within that population [3]. Obviously the method does not predict who will die or have serious complications—only the odds.

See also page 226.

Unfortunately, identification of independent risk factors requires a substantial database, which must be objectively analyzed using modern statistical methods (eg, multivariate logistic regression). Our literature generally fails to provide the data needed for these calculations. This is a serious deficiency that prevents objective assessments of risk for future patients. The deficiency also frustrates objective comparisons of results reported on similar patient cohorts from different surgical teams. Within even well-defined populations of consecutive patients, the number and severity of risk factors can vary widely. Chi square, Student's t, and analysis of variance statistics do not identify independent risk factors. More powerful statistics applied to larger populations of patients are needed. But why bother?

Almost any ethical standard requires careful and objective decision-making before high-risk operations are prescribed. Ergo the need for objective risk assessment and objective estimates of the "odds." For symptomatic patients for whom the benefits of operation are clear, low-risk operations are easily prescribed. Because the outcome is usually happy, there is less need for risk assessment; the probability of benefit far outweighs the probability of permanent morbidity or death. Not so with high-risk operations. Higher probabilities of undesirable results force consideration of continued medical management [4] or alternative therapies [5, 6].

In the past, experienced surgeons have reduced mortality and morbidity of various elective cardiac operations by patient selection. In effect, these surgeons subjectively assessed risk and more often than not denied operation to high-risk patients. Their results reflected their expertise as selectors as well as their skills as surgeons. However, if their data were analyzed with respect to the presence or absence of independent incremental risk factors, their selected experience could be compared with unselected experiences of others. Personal statistics take on more meaning when independent incremental risk factors of the operated patients are included in the analysis.

We are now in an era in which increasing numbers of high-risk patients are considered for open heart operations. Is it ethical for cardiologists or cardiac surgeons to deny high-risk patients operations because of high risk? With rare exception, cardiac surgeons survive their operations; the patient, not the surgeon, bears the risk. Should not the patient together with his or her family, cardiologist, and surgeon consider all therapeutic alternatives when a decision is needed? Complete review of the data usually makes the best course obvious. This process permits high-risk patients to have operations that may be their only hope for quality living. These patients are often the ones who benefit most [7].

High risk has always been associated with the frontiers of cardiac surgery, but in the past relatively few patients and few cardiac surgical centers were involved. Not so now. The ubiquity of coronary arterial disease, the profusion of cardiac surgical centers across the world, the development of alternative interventional therapies, and an aging population have encouraged increasing numbers of cardiac surgical groups to treat high-risk patients even though manpower and hospital-based resources may be limited.

High-risk operations impose heavy obligations on both professionals and hospitals and time demands can become oppressive. Expeditious and technically expert operation enhances a smooth postoperative course but does not ensure it. After operation, high-risk patients should not be short-changed in terms of nursing hours, crisis care, expert consultants, life support systems, and other professional and material resources that may be needed. High morbidity and mortality, as reported by Deleuze and others [1, 2], does not excuse less than superintensive care and effort. In time, technical advances and concentrated efforts by dedicated groups will reduce the morbidity and

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mortality of open heart operations in octogenarians and other high-risk groups. Cosmetic improvements produced by patient selection are not part of this process.

Risk assessment, acquisition of usable databases, patient selection, personal statistics, "rights" to operations, and obligations to high-risk patients are only a few of the contemporary uncomfortable issues raised by open heart operations in elderly patients. There are many others. An increasingly well-informed public now demands both guidance and accountability from our profession. Is it not time to openly address and discuss these and other "uncomfortable issues"?

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Oxygenated Cardioplegia: Blood Is a Many Splendored Thing

Gerald D. Buckberg, MD

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This issue of *The Annals* contains a report by Coetzee and associates [1] that focuses on the role of oxygen in myocardial protection strategies by comparing oxygenated cardioplegic solutions delivered in either a crystalloid or a blood vehicle. The absence of a nonoxygenated cardioplegic group for comparison is of no concern, as the intentional exclusion of oxygen from cardioprotective solutions makes little sense physiologically and deprives the heart of its principal substrate for energy production during cardioplegic infusions. This editorial is written to call attention to the importance of experimental models and methods in interpreting results and to emphasize that blood provides many potential benefits in addition to its capacity to enhance oxygen delivery.

The use of a nonhuman primate and the evaluation of post-bypass function in the intact heart without artificial control of preload, afterload, and heart rate adds clinical relevance to this study. Unfortunately, the cardioplegic solutions were dissimilar in more than erythrocyte content, so that differences in cardioplegic calcium, magnesium, pH, and other components may have influenced results in uncertain ways. More importantly, normal hearts arrested for only 90 minutes with multidose cardioplegia would be expected to recover ventricular performance completely, especially as prior studies of both oxygenated crystalloid cardioplegia and blood cardioplegia show this after 4 to 6 hours of aortic clamping [2–4].

See also page 230.

Coetzee and associates use pressure–volume loops to assess functional results and report decreased postischemic recovery with both cardioplegic vehicles, albeit slightly less with oxygenated crystalloid cardioplegia. The failure to recover completely after a relatively brief ischemic episode suggests a deficiency either in the cardioplegic solutions or their method of delivery or in the method of functional analysis. The pressure–volume loop method was developed in isolated, denervated hearts and cannot be used routinely in clinical practice because it requires instantaneous measurement of ventricular dimensions, and it has several limitations which have been enumerated previously [5]. Conversely, stroke work can be measured routinely, and their data show that oxygenated crystalloid cardioplegia resulted in only 61% recovery of left ventricular stroke work and slight increase in left ventricular end-diastolic pressure, whereas blood cardioplegia allowed near complete (82%) return of left ventricular stroke work at slightly lower filling pressures. These findings suggest that oxygenated crystalloid cardioplegia resulted in mild functional depression, which was avoided by use of blood cardioplegia.

The capacity of any cardioplegic solution to prevent ischemic damage and to allow total recovery of a normal heart should be a minimum requirement of any cardioprotective technique, especially as cardiac operations must now be undertaken in increasing numbers of patients with preoperative ventricular dysfunction. I believe that the normal heart model has very limited value in studies of myocardial protection and should be used *only* to test the safety of cardioplegic solutions and their methods of delivery, so that subsequent studies can be carried out on experimental models sustaining acute or chronic ischemic/hypoxic damage to simulate the types of hearts requiring cardiac operations. Study of such models offers the prospect of revealing metabolic changes that allow for the development of more comprehensive strategies for the expanded use of cardioplegic solutions to resuscitate the heart before it must undergo ischemia, as well as limit or avoid and reverse ischemic/reperfusion damage before and after unclamping [6].

The importance of using a damaged heart model is emphasized by studies showing that the same multidose cold blood cardioplegic solution that allows complete recovery after 4 hours of aortic clamping in normal hearts [2] has no resuscitative value in energy-depleted hearts even though it prevents further damage [7]. Conversely, administration of warm substrate-enriched blood cardioplegia during cardioplegic induction and reperfusion restores near normal postischemic function to energy-depleted hearts subjected to prolonged aortic clamping [7]. A recent clinical report by Kirklin [8] emphasizes the important adjunctive role of warm blood cardioplegic reperfusion in prolonging the safe duration of aortic clamping and other studies document the salutory effects of warm substrate-enriched blood cardioplegic induction and reperfusion in high-risk patients undergoing urgent revascularization [9, 10] and suggest these strategies may promote early return of contractile function in patients with acute evolving infarction after naturally occurring or percutaneous transluminal coronary angioplasty–caused coronary occlusion [11, 12].

Oxygen carriage is only one attribute of blood cardioplegia, and some others are enumerated below. Cold

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crystalloid cardioplegia certainly may deliver sufficient oxygen to meet the very low oxygen requirements of the cold arrested heart, but it cannot provide enough oxygen to meet the higher metabolic needs for cellular repair when warm blood cardioplegic induction and reperfusion are given to damaged hearts in which oxygen requirement and uptake exceed basal demands markedly [7]. Delivery of additional oxygenated cardioplegic solutions during warm induction and reperfusion does not prolong ischemic time because the heart is oxygenated during their administration, but it does increase the total cardioplegic dose. Consequently, systemic hemodilution may be accentuated if large volumes of oxygenated crystalloid cardioplegic solutions are added to an extracorporeal circuit primed with clear fluid. In contrast, iatrogenic hemodilution is minimized with blood cardioplegia, especially with a 4:1 blood cardioplegia mixture in which only 600 mL of crystalloid solution is used to deliver 3,000 mL of blood cardioplegia. The protein content of the blood vehicle provides the cardioplegic solution with naturally occurring onconicity, thus minimizing myocardial edema while simultaneously limiting the whole body interstitial water gain that may accompany the reduced oncotic pressure produced by systemic hemodilution.

An additional advantage of a blood cardioplegic vehicle is ensurance of the buffering capacity of blood proteins, especially histadine imidazole groups [13]. Furthermore, the rheologic benefits on the microvasculature afforded by erythrocytes enhance papillary muscle perfusion compared with oxygenated crystalloid cardioplegia and reduce coronary vascular resistance and edema formation [3]. The erythrocytes of blood cardioplegia also contain abundant endogenous oxygen free radical scavengers (ie, superoxide dismutase, catalase, and glutathione) [14], which may reduce oxygen-mediated injury during reperfusion. Our experimental studies show that the salutary effects of controlled blood cardioplegic reperfusion are impaired markedly when endogenous red blood cell glutathione and catalase are blocked pharmacologically [15].

The aforementioned benefits of enhanced oxygen carrying capacity, active resuscitation, avoidance of reperfusion damage, limitation of hemodilution, provision of onconicity, buffering, rheologic effects, and endogenous oxygen free radical scavengers enumerate only the known benefits of using blood as the vehicle for delivering oxygenated cardioplegia. I am confident that further studies will reveal other naturally occurring blood components (ie, enzymes, cofactors, substrates, electrolytes) that are important and would otherwise need to be added to any artificially constructed solution.

The versatility of blood cardioplegia provides the cardiac surgeon with an extremely powerful tool to actively treat the jeopardized myocardium as well as to prevent ischemic damage. No exogenous blood is needed to deliver blood cardioplegia, as a readily available blood source exists within the extracorporeal circuit during all cardiac operations when the patient's blood volume mixes with the clear priming fluid. The decision to use this valuable adjunct must be made by the cardiac surgeon, who may then select either to fashion a delivery system with tubing connected to a simple coil immersed in warm or cold fluid or to use one of many systems constructed with efficient miniaturized heat exchangers. The expense of depriving the patient of the potential benefits of blood cardioplegia includes increased perioperative mortality, prolonged intensive care unit stays, and development of late cardiac fibrosis owing to necrosis caused by less adequate protection, and far outweighs the monetary cost of its use.

My appreciation for the fact that "blood is a many splendored thing" increases as data about its salutary effects accumulate. I cannot help but wonder how future generations of cardiac surgeons will view this phase of our growth in which we must defend the use of the blood environment that normally surrounds the myocyte before and after we interrupt coronary flow for surgical convenience.

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Paraplegia Associated With Thoracotomy

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The unexpected appearance of paraplegia after routine thoracotomy for conditions unrelated to the spine or spinal cord is a surgical disaster of the highest order. Although all sorts of cerebrovascular accidents can occur during general anesthesia, and produce a wide variety of clinical neurologic syndromes, it remains that paraplegia is almost always related to a local condition affecting the spinal cord rather than an intracerebral event. Postthoracotomy paraplegia, therefore, of necessity imputes a *local* causation—although spontaneous or iatrogenic interruption of the blood supply to the cord is a local explanation possible in theory, it seems that a much simpler mechanism of injury does in fact occur, and every thoracic surgeon should be aware of the potential hazard.

In the past 2 years I have reviewed the records of 3 patients, with three different surgeons in three different hospitals, in whom iatrogenic paraplegia developed after a routine thoracotomy, and in each instance the mechanism seemed the same. All 3 patients were in the fifth or sixth decade of life and were in good general health but were undergoing operation for localized bronchogenic carcinoma. In each instance, there was persistent arterial bleeding from the intercostal vessel at the posterior end of the incision between the ribs, and normal operative maneuvers failed to stop the bleeding. In each instance, the surgeon packed hemostatic gauze into the angle between the ribs and left the gauze in place at the end of the thoracotomy.

See also page 288.

Two of the patients were paraplegic when they awoke from their anesthetic; in the third a progressive neurologic deficit developed and terminated in paraplegia hours later. In each instance, the thoracic surgeon seemed reluctant to ascribe the neurologic problem to the recent operation, producing rather long delays before neurosurgical exploration. In all 3 patients, the hemostatic gauze was found within the spinal canal, and in fact in two instances the dura had been disrupted and the gauze was found intradurally. There was no clinically significant recovery of neurologic function in any of the patients, with a variety of the usual complications of paraplegia including important medicolegal sequelae.

Although we have been unable to identify prior case reports in a computer-directed literature survey, three examples in less than 2 years in a relatively small geographic area suggest that the problem is common enough to warrant real consideration.

I suspect that most thoracic surgeons are conscious of the proximity of the spinal cord to the posterior end of intercostal incisions, in particular with respect to the use of the electrocautery. That this proximity is composed of millimeters rather than inches may not be well recognized, however. It is important also to realize that there is not a strong musculoosseous barrier protecting the spinal cord but in fact an intervertebral foramen that will admit not only the tip of the electrocautery but also a moderate-sized mass of hemostatic gauze propelled by tissue forceps.

Hemostatic gauze per se is not to be condemned because of this experience—it can be very useful in many situations in the chest, particularly after cardiac operations—but as it swells considerably when left in situ, it cannot be left in confined spaces such as the spinal canal lest it produce compression of the normal structures.

Another important observation from these 3 unfortunate patients was the low levels of diagnostic acumen and inductive reasoning exhibited by those involved. Failure to remember that paraplegia has a local cause and, even more importantly, a reluctance to accept that there was a neurologic problem, that the operative procedure could have produced it, and that a response was required contributed substantially to the delays in involving the neurosurgeons. Experimental evidence and clinical observation suggest that the neurologic damage of cord compression is time-dependent and therefore requires as rapid relief as possible to optimize the potential for recovery.

In addition to avoiding this particular iatrogenic disaster, it is incumbent on all of us to remember that unexpected complications do occur. They must be met with a forthright, open-minded, rational approach and with an ability to accept that we may have erred, unlikely though this latter may seem to each of us in the heat of the moment.

Editor's Note

Doctor Walker's important article was received by *The Annals* some time ago. Because the experiences he recounts were derived from a review of medical records, *The Annals* felt it would be helpful to have further details. We solicited a first-hand account of these cases, and Dr H. David Short was willing to act as spokesman for the surgeons involved. His contribution appears on page 288. Finally, we asked Associate Editor Dr John R. Benfield to comment about this rare but devastating complication of a universally performed operative procedure.

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Long-Term Results of Total Repair of Tetralogy of Fallot in Childhood

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Between 1958 and 1977, 170 children aged 10 years or less underwent total repair of tetralogy of Fallot at The Johns Hopkins Hospital. Follow-up data were obtained on 128 (90%) of the 143 who survived the operation at 10 to 28 years postoperatively (mean follow-up, 18 years). All patients completed an extensive questionnaire, and 59 returned for a thorough evaluation consisting of a history and physical examination, electrocardiogram, 24-hour Holter monitoring, exercise stress testing, pulmonary function testing, and two-dimensional and Doppler echocardiography. Late survival was excellent with only two of four known late deaths due to cardiac-related causes and with all 59 patients in New York Heart Association class I or II. None had cyanosis or clubbing. Normal sinus rhythm was present in 90%. One patient had complete heart block, and 75% had right bundle-branch block on the electrocardiogram. Right ventricular function was normal by echocardiography in 78%. Residual mild to moderate pulmonary stenosis was noted by Doppler study in 8 patients. Pulmonary regurgitation was present in 78%, but in only 11 patients was it graded as moderate and in none was it severe. Stress testing documented the excellent functional status of most patients, with 92% of predicted exercise time and 94% of maximum heart rate being attained. In the few who had impaired cardiac performance, this correlated best with moderate pulmonary regurgitation. Although the overall late functional status of patients undergoing repair in the first decade of life was very good, these patients need continued follow-up to assess the severity of pulmonary regurgitation and the need of possible intervention.

(Ann Thorac Surg 1990;50:179–85)

In 1954, C. Walton Lillehei and his team successfully performed the first complete repair of tetralogy of Fallot [1]. Other surgical teams followed suit soon thereafter, and an excellent opportunity now exists for long-term evaluation of the complete repair of this complex congenital heart defect. Several reviews [2–7] have demonstrated the overall excellent operative results, even in patients operated on early in this surgical experience. These studies, however, included many patients who underwent repair as adults after the effects of long-standing right ventricular hypertension and hypoxia could have caused irreversible changes.

The present study was designed to prospectively examine the long-term functional results of total correction performed specifically in childhood, as this is the currently accepted practice. The study includes only children who underwent repair by the age of 10 years and for whom a follow-up of at least 10 years could be obtained so that it would truly be a long-term follow-up of total repair performed in childhood before maturation had taken place.

Material and Methods

Between 1958 and 1977, 170 patients aged 10 years or less underwent total repair of tetralogy of Fallot at The Johns Hopkins Hospital. Tetralogy of Fallot was diagnosed when patients had (1) right ventricular pressure of at least 85% of left ventricular pressure, (2) pulmonary artery pressure of less than or equal to 25 mm Hg, and (3) aortic/femoral artery saturation of less than or equal to 93% or dye-dilution curves confirming right-to-left shunting at the level of the ventricular septum.

There were 27 perioperative deaths; thus, 143 patients were available for follow-up. There were only four known late deaths, two of which were of cardiac-related causes (one from progressive heart failure and one from subacute bacterial endocarditis at 8 and 12 years postoperatively, respectively). Eight patients are known to be alive but further information could not be obtained, and 15 other patients, most of whom were thought to be living outside the United States, could not be contacted at all. Thus, of the 124 known survivors, 116 were contacted (Fig 1). Each completed the study questionnaire.

The patients in the study were evaluated 10 years to 28 years 5 months postoperatively (mean follow-up, 17.8 ± 4.9 years). Surgical correction was performed at a mean age of 7.5 ± 2.4 years (range, 1.5 to 10 years). Age at follow-up ranged from 12 to 37 years (mean age, 25 ± 6.3 years).

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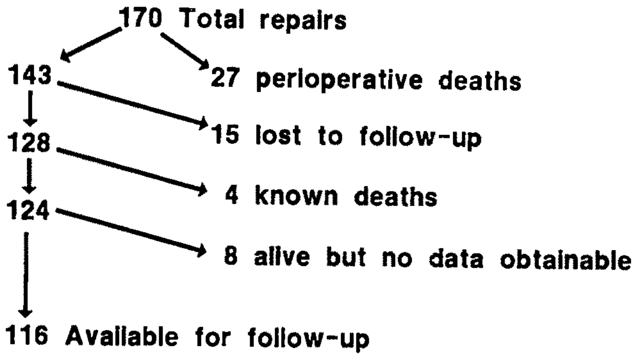

Fig 1. Availability of and outcomes for the 170 patients who underwent total repair of tetralogy of Fallot at Johns Hopkins between 1958 and 1977.

Of this total group of 116 patients, 59 agreed to return to Johns Hopkins for examination and noninvasive testing. Because of the extensive nature of the testing, the size of this follow-up group had to be limited to the first 60 responders, 59 of whom ultimately returned and completed the evaluation. This evaluation consisted of a complete physical examination, an electrocardiogram, 24-hour Holter monitoring, exercise stress testing, pulmonary function testing, and two-dimensional and Doppler echocardiography. In addition, for many of these patients, preoperative and postoperative catheterization results were available.

Data were collected according to a strict protocol over a 6-month period. Doppler and two-dimensional echocardiography were performed using a Hewlett-Packard model 77020A instrument (Andover, MA) by a single technologist under the supervision of one of us (K.Z.) [8]. Exercise stress testing was performed according to the Bruce protocol with respiratory gas exchange measurements and was also directly supervised by one of us (S.R.). Twenty-four–hour ambulatory electrocardiographic monitoring was performed using a Delmar 445 reel-to-reel recorder (Irvine, CA) and scanned on a Delmar model 750 innovator scanner.

Operative Technique

All patients underwent repair through a vertical right ventriculotomy with closure of the ventricular septal defect and placement of a right ventricular outflow tract patch of Teflon, Ivalon, Dacron, or pericardium as previously described [9]. Forty patients had had previous palliative shunts, the right Blalock-Taussig shunt being the most common (Table 1). The mean length of time the shunt was in place before takedown at total correction was 6.0 ± 2.0 years. Five patients required subsequent closure of a residual ventricular septal defect. One patient required subsequent replacement of the tricuspid valve and implantation of a permanent artificial pacemaker. A review of the operative reports for the 59 patients returning for in-depth examination revealed that 39 of these patients had had primary closure of the right ventricular outflow tract, 10 had undergone transannular patching, and the rest had had isolated pulmonary artery or subvalvar patching only. All patients had undergone infundibular myotomy-myectomy.

The 59 patients who returned for this detailed evaluation make up the core of this study, but they were similar to the total group of 116 in terms of sex distribution, presence of a previous shunt, general health status, dates of operation, and age range. There were no differences in mean interval from time of correction to time of follow-up or in mean age at follow-up. The only significant difference between these two groups was that the patients who returned for further evaluation had had repair at a slightly older age, the mean age of this group being 8.1 ± 2.2 years at the time of total correction versus 6.9 ± 2.6 years ($p < 0.02$) for the total group. Therefore, the 59 patients are thought to be representative of the entire group of patients available for follow-up.

Statistical Analysis

Statistical analyses were performed using the χ^2 test and the Wilcoxon rank sum test (for nonparametric variables). A paired t test was used for continuous variables. The results are presented as the mean ± the standard deviation. All statistical analyses were performed using the SAS program [10]. Informed consent as approved by this institution's Joint Committee for Clinical Investigation was obtained from each of the patients who returned for noninvasive testing or their legal guardians.

Results

Questionnaire Data

One hundred two (88%) of the 116 patients were in good to excellent health at follow-up. Eighty-three percent of the patients required no medicines at all, and only 2 patients were on a regimen of digoxin or diuretics. None required antiarrhythmic medications, and only 2 (1.7%) had had a stroke. Two patients were on a regimen of anticoagulants.

Ninety-eight of the 116 patients or 84% were employed full time or were in school (Table 2). Forty had had a high-school education, 38 had completed or were in college, and 7 had received graduate degrees. Nineteen of the 56 female respondents had had a total of 28 children, and 12 of the 60 male respondents had had at least 1 child. Three of the patients had become nurses and 1, a phle-

Table 1. Type of Shunt and Duration of Placement Preoperatively

Shunt	No. of Patients	Duration[a] (yr)
Right B-T	25	5.9 ± 1.7
Left B-T	8	5.6 ± 2.7
Waterston	2	3.1 ± 0.8
Potts	3	7.9 ± 1.0
Other	2	9.2 ± 0.9

[a] Data are shown as the mean ± the standard deviation.

B-T = Blalock-Taussig anastomosis.

Table 2. Results From Questionnaires Sent to 116 Patients

Variable	No. of Patients[a]
Health, good to excellent	102 (88)
No medications necessary	96 (83)
Full-time employment or in school	98 (84)
Education level	
High school	40
College	38
Graduate school	7
No. of female patients with children	19/56 (34)

[a] Numbers in parentheses are percentages.

botomist. Seventeen (15%) had required rehospitalization at some point other than for routine postoperative catheterization, and 10 (9%) had required more than two rehospitalizations.

Follow-up Examination

Of the 59 patients who returned for follow-up examination, 55 were found to be in New York Heart Association class I and 4 in class II. Three were noted to have occasional episodes of syncope, and 13 related a history of irregular heart beat. There had been no documented episodes of myocardial infarction.

On physical examination, the patients had normal blood pressures with a mean value for the group of 116/88 ± 14/12 mm Hg. None had cyanosis or clubbing. None had overt signs of congestive heart failure.

Catheterization Data

Of the 59 patients who returned for examination, preoperative catheterization data were available on 37 and catheterization data obtained after total correction, on 43. Right ventricular systolic pressures fell from a mean of 95 ± 17.9 mm Hg preoperatively to 35.5 ± 12.8 mm Hg after correction ($p < 0.0001$). Diastolic right ventricular pressures also dropped significantly from 5.9 ± 3.1 mm Hg to 4.95 ± 3.0 mm Hg ($p < 0.01$). Although systemic oxygen saturation also appeared to rise from a mean of 78.7% ± 17.1% to 96.0% ± 1.7%, this did not reach significance ($p = 0.15$), a finding most likely due to the small number of patients and large range of values before correction. At catheterization after repair, pulmonary regurgitation was absent in 24 (60%) and was rated as mild in 8 (20%), moderate in 7 (17.5%), and severe in 1 (2.5%). Tricuspid regurgitation was absent in 37 (92.5%) and was rated as mild in 2 (5%) and severe in 1 (2.5%). There was evidence of a residual ventricular septal defect in 7 patients (16.2%).

Electrocardiography and Holter Study

On the follow-up electrocardiogram, 53 patients (90%) were in normal sinus rhythm, 4 had first-degree atrioventricular block, and only 1 was in complete heart block. Forty-four (75%) demonstrated complete right bundle-branch block, and 7 additional patients had incomplete right bundle-branch block. Only 1 patient had completely normal conduction, and the remaining 7 patients had various other forms of intraventricular conduction delays.

Twenty-four–hour Holter studies demonstrated a mean heart rate of 78.6 ± 10 beats/min. Fourteen patients (24%) demonstrated multiple forms of premature ventricular contractions, and 2 had brief runs of ventricular tachycardia. Five had episodes of transient second-degree heart block. All but 12 patients had some premature ventricular contractions with a mean frequency of 23 ± 58 per 24 hours. Twenty-nine had ventricular bigeminy or couplets. Atrial ectopy was less frequent with only one run of supraventricular tachycardia being recorded and a mean of 6 ± 17 premature atrial contractions per 24 hours in 28 patients.

Stress Test and Pulmonary Function Testing

Stress test data were collected on 55 patients who were able to exercise a mean of 10.8 ± 2.3 minutes, which was 92% of predicted, and achieve a maximal heart rate of 182 ± 14 beats/min, which was 94% of predicted. No exercise stress tests were stopped because of arrhythmias, although 23 patients had premature ventricular contractions on exercise, including 5 patients with multifocal contractions and 4 with ventricular couplets or triplets. Pulmonary function testing revealed a normal mean forced expiratory volume in 1 second of 2.9 ± 0.8 L but a mean forced vital capacity of 3.5 ± 1.1 L, which was only 82% of predicted.

Two-Dimensional and Doppler Echocardiography

Right ventricular function was rated as normal in 46 patients (78%), mildly depressed in 12 (20%), and moderately depressed in 1 patient (2%). Thirty-seven patients, or 63%, demonstrated abnormal septal motion. There was some Doppler evidence of residual ventricular septal defect in 8 patients. Some pulmonary regurgitation was present in 46 (78%), but in only 11 was it graded as moderate and in none as severe. A right ventricular outflow tract gradient of greater than 15 mm Hg was found in 9 patients (15%) with ranges of 16 to 56 mm Hg. Thirty-seven patients, or 63%, had some evidence of tricuspid regurgitation, but the regurgitation was rated as moderate in only 5 (8.4%) (Table 3). No major mitral regurgitation was found, and only 1 patient had moderate aortic insufficiency. Two patients had pulmonary valve calcifications, 1 had mild subvalvar pulmonary stenosis, and 3 had mild to moderate supravalvar pulmonary stenosis. The right ventricular diastolic area was 21.8 ± 6.3 cm^2, and the right ventricular systolic area was 15.1 ± 4.4 cm^2.

Correlations

Patients with moderate to severe pulmonary regurgitation had a significantly increased right ventricular diastolic area ($p = 0.008$), which in turn was associated with a decreased exercise duration ($p = 0.02$), a decreased forced vital capacity ($p = 0.03$), and the occurrence of premature ventricular contractions during exercise ($p = 0.004$) and on recovery ($p = 0.0001$). Moderate pulmonary regurgitation

Table 3. Results of Doppler Echocardiography in 59 Patients

Finding	No. of Patients[a]
Residual VSD	8 (14)
Pulmonary regurgitation	
Mild	35 (59)
Moderate	11 (19)
Pulmonary gradient	9 (15)
>15 mm Hg (range, 16–56 mm Hg)	
Tricuspid regurgitation	
Mild	32 (54)
Moderate	5 (8)

[a] Numbers in parentheses are percentages.

VSD = ventricular septal defect.

was directly associated with a decreased exercise duration ($p = 0.04$), the occurrence of premature ventricular contractions after stress testing ($p = 0.02$), a higher New York Heart Association class ($p = 0.03$), the occurrence of ventricular couplets or bigeminy ($p = 0.01$), and the need for medications ($p = 0.001$). Moderate pulmonary regurgitation was also associated with transannular patching ($p = 0.06$).

Despite right ventricular outflow tract patching, the mean outflow gradient was significantly higher for those patients who had patching versus those who did not (13.3 ± 13.8 mm Hg versus 7.5 ± 5.3 mm Hg; $p = 0.03$). Increased right ventricular outflow tract gradient did not correlate with right ventricular diastolic area or the occurrence of ventricular ectopy or decreased ventricular performance. Age at time of repair was not significantly associated with exercise performance or the occurrence of ventricular ectopy. Patients who were older at the time of repair were found to be more likely to require transannular patching ($p = 0.06$) and were more likely to have required a palliative shunt before total repair ($p = 0.02$).

Comment

When Alfred Blalock [11] reported the first surgical therapy for tetralogy of Fallot in 1945, he provided hope for many children whose condition had previously been considered untreatable. The Johns Hopkins Hospital became an international referral center for the treatment of patients with tetralogy of Fallot, and an extensive early experience with the management of this anomaly using systemic–pulmonary artery shunting was acquired. The pioneering efforts of Lillehei in direct repair of tetralogy of Fallot defects in 1954 were soon followed by "total corrections" at other centers, including Hopkins. The patient group described in the present study is, in fact, only a small proportion of the more than 500 patients having total repair of tetralogy of Fallot done at Johns Hopkins during this period.

Most of the total repairs undertaken in the early years of this study were performed in children more than 10 years old [12]. The present study group of younger patients is, therefore, a select one. It likely includes both those children who were considered anatomically excellent candidates for total repair as well as those who were not adequately palliated with a shunt. Notwithstanding such inclusion biases, this study demonstrates the overall excellent late status of this group of patients. By limiting this late follow-up review to children who had undergone total repair by the age of 10 years, it was hoped that data would be generated that could be extrapolated to some extent to the current practice of early definitive repair of tetralogy of Fallot in children.

Although the present study does provide some of the longest follow-up information on children who have had total repair of tetralogy of Fallot, the mean age of these patients at the time of this follow-up was only 25 years. Clearly, these data, though encouraging, may not provide reliable projections of late survival or life-span expectations. Most patients included in the present review have achieved a good functional status, attaining normal educational and vocational goals. Eighty-five percent of the patients have required no further hospitalizations other than for follow-up catheterizations, which were routinely performed in the early years of the study. The data from this study, however, do demonstrate an association between moderate pulmonary regurgitation and increased right ventricular size, the development of arrhythmias during exercise, and decreased exercise capacity, suggesting that further operation may be necessary to correct residual pulmonary regurgitation in some of these patients.

It is difficult to determine the time course of the development of right ventricular abnormalities, as such changes are similar or related to problems already present in patients with tetralogy of Fallot at the time of the initial operation [13]. It has been suggested that total repair should be undertaken early in childhood to avoid irreversible right ventricular damage [14–16]. Although the association of pulmonary regurgitation and right ventricular dysfunction is clearly established in this study, it is not known whether both conditions have coexisted in these children or whether there has been a progressive cause and effect relationship. A previous study [12] from this hospital, which reported catheterization data obtained at an average of 9 years after repair, suggested that major pulmonary regurgitation was well tolerated, at least up to that postoperative interval. Although that study used only catheterization data and included patients having repair at all ages, one can infer that though pulmonary regurgitation was not associated with altered functional status at that 9-year follow-up, this association has clearly been established in the present study at 18 years' follow-up, thereby suggesting a progressive detrimental effect of pulmonary regurgitation.

Previous studies [17–21] have correlated residual right ventricular outflow tract obstruction with arrhythmias and late death after complete repair of tetralogy. The lack of such an association in the present study group may reflect a surgical bias at this institution to attempt complete relief of outflow tract obstruction and to err on the side of pulmonary insufficiency. This bias is reflected by the fact that 78% of the patients in this follow-up study had evidence of pulmonary regurgitation, and only 15% demonstrated major residual outflow tract gradients.

The noninvasive analysis of cardiac function provided by exercise stress testing and echocardiography as performed in this late follow-up study may provide an excellent means by which to continue late surveillance of these patients. A satisfactory functional status at the current follow-up has allowed most of these patients to follow nearly normal life-styles, but residual cardiac defects such as pulmonary regurgitation, even though generally well tolerated, may limit long-term functional stability. Therefore, the results of this study suggest that regular late follow-up evaluation should be continued indefinitely in patients who have had complete repair of tetralogy of Fallot defects.

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DISCUSSION

DR HARVEY W. BENDER, JR (Nashville, TN): I enjoyed this presentation very much and thank Dr Horneffer for the opportunity to review the manuscript before his presentation. As expected, the presentation was very clear and well illustrated.

The information provided from the Hopkins group should be very important in the continued follow-up of patients with the tetralogy malformation. This report represents long-term follow-up of many patients who were included in a very important report in 1962 by Drs Henry Bahnson and Frank Spencer demonstrating that this was a procedure that could be carried out with acceptable mortality figures.

I am particularly pleased to have the opportunity to discuss this report because I was involved in the care of many of these patients during my tenure as a resident and staff surgeon.

I have a couple of observations and two questions for Dr Horneffer. First, we should recognize that this is a select group of patients and that most of the data are derived from 59 of 170 patients, 27 of the total having died in the perioperative period. Horneffer and associates think that the 59 patients are representative of their 124 known surviving patients. Although this may be true, I am not sure that we can reach that conclusion. If it is valid, we can take some comfort in the fact that, in general, these patients have done well over the long term.

The two most worrisome findings are the significant incidence of pulmonary regurgitation associated with right ventricular mechanical problems, which may be the harbinger of future operations, and the number of patients with arrhythmias, particularly those ventricular in origin. On Holter monitoring, all but

12 patients had premature ventricular contractions. Twenty-four percent had multiform premature ventricular contractions and 29 of 59 had bigeminy or couplets. It is likely that this will be of greater importance in the next decade.

The first question I have is related to the data derived from the questionnaire and their correlation with the data from the 59 studied patients. How many of the patients found to have pulmonary regurgitation and depressed ventricular mechanics or ventricular arrhythmias were in the group of patients reporting their health as good or excellent and requiring no medication?

My point is that many patients surviving a corrective operation for congenital defects could have the impression that their prognosis is better than it actually is. I think we will continue to see arrhythmias complicating the long-term course of patients who had an intracardiac operation. This should encourage us to strive to develop simple, precise techniques in the repair of these defects and to produce the least myocardial damage possible. This brings up the second question.

As these patients were repaired over a 19-year period, the method of myocardial protection ranged from coronary artery perfusion without aortic cross-clamping through intermittent cross-clamping, hypothermic ischemic arrest, and potassium cardioplegia. Dr Horneffer, did you find any correlation between the type of myocardial protection and the incidence of ventricular arrhythmias?

DR ADNAN COBANOGLU (Portland, OR): When my colleagues and I recently reviewed our experience with tetralogy of Fallot, particularly late results, at the Oregon Health Science University, there were 268 patients. I was happy to see that a similar number of patients to that in the present study had had operative intervention before 1978.

It is of note that 90 of our patients were less than 1 year of age at the time of primary correction. So this series represents both patients operated on at an early age and truly late-term results. The actuarial survival of these patients in the long run was excellent. At 15 and 20 years of follow-up, 85% of these patients were alive. Though Horneffer and associates did not show an actuarial survival curve, they indicated similarly good survival.

As far as indicators of long-term survival in these patients are concerned, we looked at year of operation, age, ventriculotomy, transannular patch, weight at the time of operation, intraoperative use of inotropic agents, and tetralogy spells before operation, and found that none of these had an effect on long-term survival. Long-term exercise tolerance has been excellent. Eighty percent of the patients have good to excellent exercise tolerance, but some have not fared as well. To our surprise, a transannular patch, which would mean pulmonary regurgitation, did not have an effect on long-term exercise tolerance, whereas a ventriculotomy did.

I congratulate Horneffer and associates, and agree that it is very important to continue a detailed analysis of right ventricular performance in tetralogy patients 10, 15, and 20 years after total correction.

I have a few questions. What was the reoperation rate in this series? I may have missed this information during presentation.

Were there any patients who needed pulmonary valve implantation during late follow-up? And based on this detailed analysis, would you have recommendations as to when to go back in to implant a pulmonary valve?

DR C. WALTON LILLEHEI (St. Paul, MN): Thirty-five years ago the reports of complete correction of tetralogy of Fallot were greeted with initial astonishment because tetralogy is such a complex malformation. That was soon followed by skepticism about the long-term outlook. Thus, it is particularly gratifying today to hear this excellent report on late results from such an important center as Hopkins. From our experience, I can add some important data about the 29- to 35-year follow-up results.

From the years 1954 through 1960, 106 patients were discharged from the University of Minnesota Hospital after total correction. Our follow-up is 99% complete (105 patients). At the time of operation, 11 patients were less than 2 years old (youngest, 4 months), 14 were older than 15 years (oldest, 45 years), 18 were 2 to 5 years old, and 63 were 6 to 15 years of age. Eighty-four of these patients are alive and well (actuarial 30-year survival is 77%). A remarkable 32% have completed college, and 10 have completed graduate school (5 with a Masters degree, 2 MDs, 2 PhDs, and 1 lawyer). Other information has been published (Ann Surg 1986;204:490). Both the youngest patient (4 months) and the oldest patient (45 years) at the time of operation are long-term survivors, and exemplify very well the excellent prognosis that these patients have experienced. The oldest patient was very cyanotic (hemoglobin, 250 g/L [25 g/dL]) preoperatively. Seven months after operation, she returned for study. She had a normal oxygen saturation, no shunts, and a pulmonary outflow gradient of 16 mm Hg. Thirty-three years after operation, she works 3 days per week repairing jewelry, and at 79 years of age, remains in remarkably good health.

The youngest patient graduated from medical school, completed graduate training, and now, 33 years after correction, is a busy general surgeon without health problems.

I am sure the first patient on whom we attempted intracardiac correction (August 31, 1954) is of interest to this group. He had been referred to us for a Blalock shunt. This first attempt was a complete success. It is now 35 years since his operation, and he is completely healthy and takes no medications. He is a professional musician and has his own band, which in 1987 was voted "The No. One Rock and Roll Dance Band in Minnesota."

I conclude with a question that has troubled us in our late follow-up studies. Five of our patients with tetralogy died suddenly and unexpectedly between 10 and 20 years after operation. None of the 5 was known to be having arrhythmias. For 3, the postoperative information was very complete: all had normal postoperative right heart catheterizations, and postmortem examination showed no objective cause of death. We remain perplexed as to how to detect these patients and prevent such sudden deaths. Do you have any ideas?

DR HORNEFFER: In addressing Dr Bender's first question, our facilities limited us to doing an in-depth evaluation on only about half, or 59, of the 116 patients to whom we sent questionnaires. These 59, however, were unselected at the time and were invited to come back before we had any results about their present health status. In comparing the variables we could, we determined the two populations were similar. However, as you point out, we do not have the same data set to be absolutely sure that they are comparable.

In terms of how many patients with moderate pulmonary regurgitation rated their general health status as good, several patients with clinically significant pulmonary regurgitation and 1 of the patients with a high residual right ventricular outflow tract gradient rated their health status as good. Those patients with pulmonary regurgitation, however, clearly performed less well on the stress test, and I think this is the determining test in evaluating present functional status.

There were insufficient data in this report to correlate myocardial protection with the occurrence of late arrhythmias.

Dr Cobanoglu, in terms of the reoperation rate, we mentioned that 5 patients required closure of a residual ventricular septal defect and 1 required insertion of a tricuspid valve. None underwent pulmonary valve implantation.

As to when to insert a pulmonary valve in patients with pulmonary regurgitation, this question has yet to be answered. On the whole, the present functional status of these patients was quite good, and we thought that on clinical grounds, none required a valve at this point. This is one of the reasons we recommend close continued follow-up, because even though this is a relatively late follow-up, the mean age of the patients returning was only 25 years. Over the years, the pulmonary regurgitation could turn out to be a very stable lesion or could get substantially worse. I do not think these data allow us to predict that at this point.

Dr Lillehei, similarly, the question of arrhythmias in tetralogy of Fallot is one that I believe we do not have the data to answer yet. There have been many studies that have reported instances of sudden death when arrhythmias are present in the face of high residual right ventricular outflow tract obstruction. Very few of our patients in this study had major residual gradients, which probably reflects a surgical bias to relieve outflow tract obstruction and err on the side of pulmonary regurgitation. Whether the occurrence of these arrhythmias needs to be treated as aggressively in patients who do not have high right ventricular pressures remains unanswered.

Notice From the Southern Thoracic Surgical Association

The Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Cerromar Beach, Puerto Rico, November 8–10, 1990. There will be a $155 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 8, 1990. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Advance registration forms, hotel reservation cards, and details regarding transportation arrangements will be mailed to Association members. Nonmembers should write to the Secretary-Treasurer, Gordon F. Murray, MD.

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Thoracoscopy and Talc Poudrage for Pneumothoraces and Effusions

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The indications, technique, and results of thoracoscopic talc poudrage in the two clinical settings of pneumothorax and recurrent pleural effusion in chronically ill patients are reported. Forty patients underwent this treatment between May 1982 and September 1989. The patients ranged in age from 10 months to 78 years. Of the 20 patients who underwent treatment of pneumothorax, 9 had cystic fibrosis, 7 had severe chronic obstructive pulmonary disease, 2 had spontaneous pneumothoraces, and 2 had postoperative parenchymal bronchopleural fistulas. Nineteen patients (95%) had successful treatment. Of the 20 patients who underwent treatment of chronic effusions, 14 had malignant etiologies, 3 had chylothoraces, and 3 had other miscellaneous effusions. Eighteen patients (90%) in this group had successful treatment. There were two hospital deaths related to the underlying disease processes after the pleural space problems were successfully treated. This study suggests that proper selection of patients and full exploitation of the capabilities of thoracoscopy and talc poudrage will result in effective treatment with low morbidity and mortality.

(Ann Thorac Surg 1990;50:186–9)

Recurrent pneumothoraces in patients with severe underlying pulmonary parenchymal disorders and recurrent pleural effusions of a noncardiac-related nature in patients with severe underlying diseases are clinical disorders in which there is a premium on avoiding major surgical intervention and at the same time avoiding recurrent similar problems. Thoracoscopy was first described by Jacobaeus in 1910 as a way of gaining access to the thoracic cavity to do limited diagnostic and therapeutic procedures without a thoracotomy [1]. This procedure fell into disuse with the effective treatment of most forms of tuberculosis by drug therapy. Within the last 20 years, however, its use has been revived in North America to remove intrapleural foreign bodies [1], diagnose the cause of pleural effusions [1], treat malignant pleural effusions [2, 3], and treat recurrent pneumothoraces [4]. Talc itself has long been known to stimulate an adhesive, obliterative pleuritis [5].

This report describes our review of the use of thoracoscopy and talc poudrage in the clinical states of both recurrent pneumothorax and recurrent pleural effusion to assess patient selection, procedural and anesthesia technique, treatment effectiveness, and complications.

Material and Methods

Forty patients underwent thoracoscopy and talc poudrage at the University of Virginia Health Sciences Center between May 1982 and September 1989 (Table 1). They ranged in age from 10 months to 78 years. In the group with pneumothorax (n = 20), 9 had cystic fibrosis (5 were previously reported from this institution [6]), 7 had chronic obstructive pulmonary disease, 2 had spontaneous pneumothorax, and 2 underwent the procedure for persistent postoperative air leak with pneumothorax. In the group with chronic recurring pleural effusions (n = 20), 14 had malignant pleural effusions, nine of which were secondary to lung cancer, two secondary to breast cancer, and one each secondary to lymphoma, ovarian cancer, and cervical cancer. Three had pleural effusions that were chylous in nature, and 3 had pleural effusions in a miscellaneous category, which included Waldenström's macroglobulinemia (a plasma cell dyscrasia resembling lymphoma), yellow nail syndrome, and a nonmalignant effusion after radiation therapy for lymphoma.

Thirty-eight of the 40 patients underwent the procedure under general anesthesia. A double-lumen endotracheal tube was used when the size of the patient permitted this option. Two pediatric patients underwent the procedure with intercostal nerve anesthesia. Patients were most commonly positioned in the lateral decubitus position, as this afforded the best view of all areas of the pleural cavity. The chest was widely prepared to allow the option of placing a chest tube or tubes in any area if adhesions or underlying diseases dictated this step.

A 9-mm trocar was inserted after the area was aspirated to confirm the presence of fluid or pneumothorax. A Storz rigid telescope (Karl Storz Endoscopy-America, Inc, Culver City, CA) was then introduced through the trocar. In the patients with pleural effusion, as much fluid as possible was removed by a suction catheter passed through the trocar before the telescope was inserted. The telescope assisted in the choice of location for insertion of the second trocar, usually 5 cm from the original position in the same interspace. Under direct visualization, a suction catheter passed through the second, or working,

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Table 1. Results of Thoracoscopic Talc Poudrage

Condition	No. of Patients	Diagnosis	Successful Treatment	Complications
Pneumothorax	20	Cystic fibrosis (9) COPD (7) Spontaneous pneumothorax (2) Postoperative air leak (2)	19 (95%)	None
Pleural effusion	20	Malignant process (14) Chylothorax (3) Macroglobulinemia (1) Yellow nail syndrome (1) Nonmalignant effusion after radiation therapy (1)	18 (90%)	1 persistent small effusion treated with tube thoracostomy 2 hospital deaths (pulmonary embolus, support withdrawal)

COPD = chronic obstructive pulmonary disease.

trocar removed any remaining pleural fluid. On occasion, a biopsy forceps or an insulated cautery was used to divide pleural adhesions that were thought to restrict lung reexpansion.

Talc insufflation over the entire pleural surface was then carried out under direct visualization through the second trocar using a Huzly insufflation system (Karl Storz Endoscopy-America, Inc) (Fig 1). The talc used was *US Pharmacopeia* talc, a hydrous magnesium silicate known in its native form as soapstone or French chalk. The talc was specified by the manufacturer (Humco Laboratory, Texarkana, TX) to be free from asbestos. The talc was incubated in a dry-heat oven at 125°C for 12 hours and then cultured to demonstrate no bacterial or fungal contamination over a 7-day period before it was released for operative use.

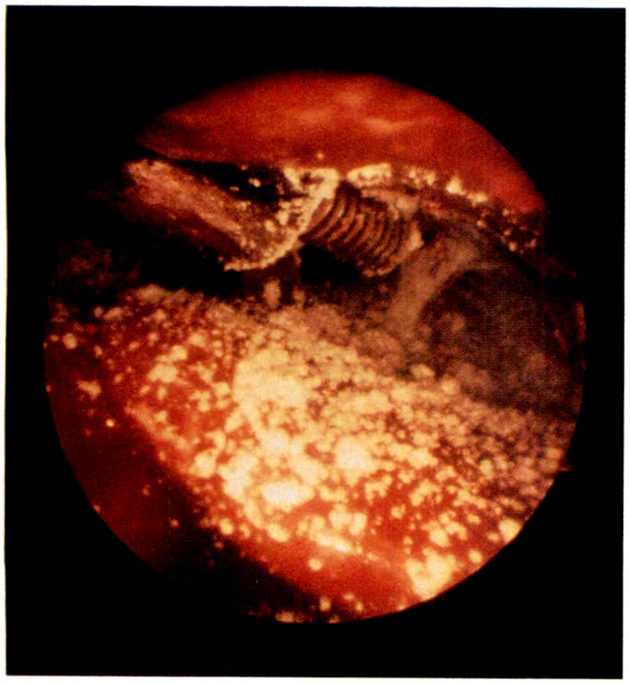

Fig 1. Intraoperative view through thoracoscope of talc on visceral pleural surface after poudrage. The insufflation catheter is seen within the working trocar at the top of the figure.

The 9-cm tube in the insufflation system was found to hold 3.5 g of talc. No more than three tubes, or 10.5 g, were used in the adult patients, and correspondingly less talc was used in the smaller pediatric patients.

Collapse of the lung to permit maximum visualization was facilitated by using single-lung anesthesia and by opening the trocar so that extra air could enter the pleural cavity. After adequate removal of fluid and division of restrictive adhesions, the pleural surfaces were covered with talc. The working trocar was removed and a chest tube inserted through that site under direct visualization with the thoracoscope. On occasion, a second tube was placed through the original trocar site for maximum drainage of air or fluid.

Results

Twenty patients were treated with thoracoscopy and talc poudrage for persistent pneumothorax, and successful leak closure was accomplished in 19 (95%). The one immediate failure was in a patient with chronic obstructive pulmonary disease with a large air leak in a moderate-sized bleb. This patient had a persistent pneumothorax and subsequently underwent limited thoracotomy and bleb resection. The 2 patients with postoperative air leak had undergone open lung biopsies for severe parenchymal disease and had chronic bronchopleural fistulas with a small associated pneumothorax. Both were successfully treated with talc poudrage. There have been no recurrences in this group, but some of the patients have died of the underlying disease since treatment.

Twenty patients were treated with thoracoscopy and talc poudrage for recurrent effusions of various causes; success was achieved in 18 (90%). These patients exhibited no recurrence during hospitalization or up to 1 month after treatment. In 2 patients with malignant effusion, the process was not controlled by talc. There were two hospital deaths in this group, both occurring after the effusions had been treated and the chest tubes removed. One death was secondary to a pulmonary embolus in a patient with underlying malignancy, and the other was in a patient with advanced lymphoma who requested that all support be withdrawn.

The average time to removal of the chest tube for the pneumothorax group was 5.2 days with a range of 2 to 24 days. The average time to chest tube removal for the pleural effusion group was 4.6 days with a range of 3 to 10 days. There were no episodes of respiratory distress syndrome or pneumonitis after intrapleural talc poudrage in this series.

Comment

This study involved the use of thoracoscopically guided talc poudrage in two separate clinical settings—pneumothorax and pleural effusion. The use of talc for the treatment of pneumothorax has been previously reported [4, 6]. Our results support a previous observation by our group [6] that recognition and lysis of pleural adhesions by the direct visualization afforded by thoracoscopy contributes to the effectiveness of this treatment of pneumothorax. The one failure in the pneumothorax group, a large leak in a clinically unrecognized bleb, leads us to recommend that the surgeon assess at the time of thoracoscopy the ability of the lung to reexpand under positive-pressure ventilation and perform a limited thoracotomy if adequate reexpansion is not demonstrated.

Patients with pneumothorax and underlying chronic lung disease generally have a longer life expectancy than patients with recurrent pleural effusions, especially those of the malignant variety. This fact raises the issue of the long-term effect of intrapleural talc. The development of malignant mesothelioma and other asbestos-related diseases is not a problem if asbestos-free talc is used. Potential pleural thickening with restrictive lung disease is a theoretical concern. Lange and colleagues [7] studied patients 22 to 35 years after talc poudrage for spontaneous pneumothorax and found only a mild restrictive impairment (total lung capacity averaged 89% of the predicted value). McGahren and co-authors [8] recently reported the effect of talc poudrage on growing swine and described an early impairment in dynamic compliance, which resolved with time and growth.

Certainly in the setting of cystic fibrosis or severe chronic obstructive lung disease, we believe talc poudrage is highly effective (95% in this series), safe, and unlikely to affect pulmonary function negatively. The pleural symphysis achieved is so effective, however, we do not recommend the use of talc if the patient could possibly be considered a candidate for subsequent lung transplantation.

The use of talc for the treatment of pleural effusions has been extensively discussed in the literature [2, 3, 9, 10]. Austin and Flye [5] reported a 90% effectiveness rate for talc compared with 80% to 87% for tetracycline pleurodesis, 60% for tube thoracostomy alone, and less than 4% for thoracentesis. Little and co-workers [11] obtained an 83% effectiveness rate with the use of pleuroperitoneal shunts for recurrent effusions, but this approach necessitates continued shunt compression by the patient or the family.

The present study confirms the effectiveness of talc poudrage. This method necessitates general anesthesia in very ill patients; the advantages, however, are several. Oakes and associates [1] pointed out the lack of pain experienced by the patient, and our experience substantiates this, especially when talc poudrage is compared with the use of intrapleural tetracycline in the awake, sedated patient. Thoracoscopy avoids a painful incision while permitting a direct visual assessment of the pleural surface. This allows lysis of adhesions where necessary and biopsy if diagnostically indicated, and affords the possibility of assessing the effect of positive-pressure ventilation on a trapped lung to see if apposition of the pleural surfaces will be possible. Failure to assess lung reexpansion may have played a role in our two failures in the pleural effusion group. Oakes and colleagues [1] described a case of malignant effusion in which recognition of a nonexpanding lung at thoracoscopy permitted immediate thoracotomy and decortication with successful obliteration of the pleural space.

Although no patient in our series experienced pulmonary parenchymal complications, the use of intrapleural talc for pleural effusion has been reported by Bouchama and co-authors [12] to cause acute pneumonitis and by Rinaldo and associates [13] to cause respiratory distress syndrome. It is known that intravenous talc can cause pulmonary hypertension and increased capillary permeability [12], but the causal relationship to intrapleural talc remains unexplained. The absence of this complication in our series may be explained by our use of the talc as a powder (poudrage) as opposed to its use in a suspension in normal saline solution as described by Bouchama [12], Rinaldo [13], and their co-workers.

The 2 deaths, one due to pulmonary embolus and the other due to the desire of the patient to terminate care, point out that these patients are often bedridden, often have underlying malignancies, and are at risk for an embolus and also that the decision to undertake thoracoscopic pleural talc poudrage should be reserved only for patients with a prospect for survival greater than 1 month. With more limited survival expectancy, we advocate repeat thoracentesis with or without a sclerosing agent.

In summary, our study demonstrates that talc poudrage is an effective treatment for pneumothorax and recurrent effusion in patients with severe underlying pulmonary disease when proper patient selection is made and when maximum use is made of the thoracoscope to identify the process, release adhesions, assess lung reexpansion, and widely distribute talc over the pleural surface.

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DISCUSSION

DR SAFUH ATTAR (Baltimore, MD): I have two comments to make, one with respect to the pain and the second with respect to the recurrence of effusion in the group treated for malignant effusions. At the University of Maryland Cancer Center, our routine has been to use tetracycline infusion into the pleural cavity, and we have had, I would say, nearly 100% success with this procedure. The reason for the success is twofold. First, we routinely use lidocaine hydrochloride, 100 mg, which is injected with the tetracycline, to relieve pain. The patients have expressed definite relief when lidocaine is administered intrapleurally with tetracycline.

Second, I think the success of the procedure depends on the enthusiasm of the treating physician as well as the cooperation of the nurses and the patient. If the patient is placed in a different position every 6 hours so that the pleural space is exposed totally to the infused tetracycline, good pleurodesis will result without recurrence of the effusion. I think if you follow these two suggestions, you will not need to use the thoracoscope and talc powder for malignant pleural effusion.

DR J. ALEX HALLER, JR (Baltimore, MD): I have no quarrel with this concept of generalized pleurodesis for patients with malignant effusions because it seems to be very effective and we do not have to worry too much about the subsequent pulmonary function. I am concerned about its use in patients with cystic fibrosis, however. Pulmonary function studies done after obliteration of the whole pleural space with various techniques showed a 20% to 25% decrease in pulmonary function because of the interference with normal dynamics of that side of the chest. To avoid this, we have used a technique involving the transaxillary operative approach with gauze irritation of just the area of the lung where there was a leaking bleb.

Have you done any pulmonary function studies of your patients before and after use of talc? In those patients who are going to survive, pulmonary function is of great consequence. I am concerned that this technique might markedly decrease pulmonary function by obliterating the whole pleural space when all you really need to do is block the area where the pneumothorax has occurred.

DR GEORGE R. DAICOFF (St Petersburg, FL): One of the more pesky problems my colleagues and I have seen, not commonly but enough to be troublesome, is pleural effusion after the Fontan procedure. Have you had any experience with this, and do you think talc poudrage might work?

DR NORMAN J. SNOW (Cleveland, OH): My colleagues and I also have problems with patients with cystic fibrosis at our children's hospital. In that group of patients, how would you prospectively apply your caveat about possible lung transplantation being a contraindication to this procedure? In the future, some of these children might be candidates for heart-lung transplantation.

DR DANIEL: Dr Attar, we all were brought up on the idea of Xylocaine (lidocaine hydrochloride) and use of a tube thoracostomy. My colleagues and I tried this method, and found it to be variably successful in some patients. Even though you administer Xylocaine and neutralize it to bring the pH into line, reexpansion of the lung still seems to be a painful process. I think we are talking about two procedures that work quite well, and the question is how fully you want the first and only procedure to work well. The inability to visualize the intrathoracic cavity, recognize adhesions, or recognize a trapped lung makes blind insertion of a tube with intrapleural tetracycline less effective than direct visualization through a thoracoscope.

Dr Haller, in the manuscript we discuss the effect of intrapleural talc on pulmonary function to the extent we have any knowledge of it, and in the literature there is an interesting article from Scandinavia by Dr Lange and colleagues [7]. They restudied patients who had had talc pleurodesis 22 to 35 years later and found there was a slight decrease to about 87% in functional residual capacity versus normal controls. The authors considered this not a clinically significant change. As for basic laboratory work, Dr McGahren and co-workers [8] from the laboratories in the Pediatric Surgery Department at the University of Virginia have done a study that will be in the *Journal of Pediatric Surgery*. They divided growing swine into two groups. In one group, they instilled talc and in the control group, they did just a thoracoscopy with no talc instillation. In the dynamic compliance measurements, they found that there were some changes initially but these appeared to totally clear as the swine grew in size. That attempt to make a laboratory model appears to suggest there is not a clinically measurable change. However, that issue is important to consider.

Dr Daicoff, we have had no experience with this technique after a Fontan procedure; therefore, I cannot comment on it.

Dr Snow, you raise an issue that we think is going to be critically important if lung transplantation, particularly double-lung transplantation in patients with cystic fibrosis, becomes very common. I think that development might lead us not to recommend such an effective procedure as talc poudrage but perhaps a limited thoracotomy or something else.

Neodymium:YAG Laser and Brachytherapy in the Management of Inoperable Bronchogenic Carcinoma

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Neodymium:yttrium-aluminum garnet (Nd:YAG) laser therapy and endobronchial brachytherapy are useful modalities in the palliation of inoperable bronchogenic carcinoma. From 1983 to 1989, 218 patients underwent a total of 371 procedures involving endobronchial brachytherapy, Nd:YAG laser therapy, or both. Group 1 consisted of 130 patients who received Nd:YAG laser therapy. Group 2 consisted of 67 patients who had endobronchial brachytherapy only. Group 3 comprised 21 patients who underwent combined endobronchial brachytherapy and Nd:YAG laser therapy. All patients had received or were receiving concurrent radiotherapy. Three late deaths occurred in group 1, and 1 death occurred in group 2. More than 80% of patients achieved a good to excellent result. When applicable, we now use combined Nd:YAG laser therapy and endobronchial brachytherapy as part of the initial management of inoperable non–small cell bronchogenic carcinoma. A detailed analysis of these patients is given.

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Carcinoma of the lung is the most common disease seen by the practicing thoracic surgeon. Based on National Cancer Institute statistics, it is estimated that there will be 170,000 new cases of carcinoma of the lung in 1990, with approximately 160,000 deaths [1]. Surgical intervention is the preferred treatment for resectable non–small cell carcinoma of the lung and represents the only chance for cure. In this group of patients, 50% or less will ultimately be candidates for surgical resection [2]. When the patient cannot undergo operation for medical reasons or is not considered a candidate for surgical intervention from an anatomical or physiological standpoint, other modalities of therapy must be considered. Conventional therapy for nonresectable non–small cell carcinoma of the lung has been combination chemotherapy, external-beam irradiation, or both. Even though the results of these palliative therapies are sometimes encouraging, the high incidence of recurrence and the relatively limited value of any treatment have made the management of lung cancer a difficult problem.

Neodymium:yttrium-aluminum garnet (Nd:YAG) laser therapy for recurrent carcinoma of the lung was introduced in 1981 in France by Dumon [3] and in 1983 in the United States by Unger and Atkinson [4]. In 1985, various types of endobronchial therapy became clinically applicable for primary or recurrent inoperable cancer of the trachea and main bronchi. These modalities included electrocoagulation, endobronchial phototherapy with hematoporphyrin and laser, and endobronchial irradiation using various radiation sources [5]. The last is known as endobronchial brachytherapy. We have found that Nd:YAG laser therapy, endobronchial brachytherapy, or a combination of both represents a very important advance in the treatment of initial and recurrent obstructing tracheobronchial lesions causing airway compromise. Our purpose is to review our experience with Nd:YAG laser therapy and endobronchial brachytherapy in the management of inoperable bronchogenic carcinoma.

Material and Methods

From 1983 to April 1989, 218 patients underwent a total of 371 procedures involving endobronchial brachytherapy, Nd:YAG laser therapy, or both. Age of the patients ranged from 24 to 86 years with a mean of 62 years. There were 154 men and 64 women. All procedures were performed on the Cardiothoracic Surgical Service of Emory University Affiliated Hospitals. All laser therapy interventions were performed by the same surgeon, and all bronchoscopic afterloading catheter placements were done by the same surgeon and two pulmonologists. The afterloading radiation management was performed by two radiologists.

Laser therapy was performed using the Nd:YAG laser manufactured by Medalius. Therapy was delivered by a flexible quartz fiber through an Olympus fiberoptic bronchoscope. All endobronchial brachytherapy was performed by surgical placement of the fiberoptic bronchoscope in the appropriate area of the endobronchial tree and placement of a No. 5 afterloading catheter through which a high-intensity iridium 192 source was put into the area by the radiotherapist. Almost all brachytherapy treatments were performed on an outpatient basis.

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The patients were divided into three groups according to the type of therapy. Group 1 consisted of 130 patients who underwent Nd:YAG laser therapy only. Group 2 consisted of 67 patients who underwent endobronchial brachytherapy only. Group 3 comprised 21 patients who had combined Nd:YAG laser therapy and endobronchial brachytherapy.

Laser Therapy

Indications for laser therapy in the 151 patients receiving it were as follows: a benign tracheobronchial lesion, 4 patients; malignant tracheobronchial lesions, 142 (116 primary and 26 metastatic); and hemorrhage of more than 300 mL, 5. The most common metastatic tumors were endobronchial renal cell carcinoma, metastatic breast carcinoma, and metastatic melanoma.

All patients admitted for Nd:YAG laser therapy underwent a standard protocol management. This consisted of a complete history and physical examination, pulmonary function test, arterial blood gas assessment, chest roentgenograms, tracheal tomograms or a computed tomographic scan with coronal reconstructions, and a coagulation profile and a type and crossmatch for blood. All patients were managed by a standard anesthesia protocol consisting of an arterial line or dynomat monitoring and finger or ear oximetry. Concentration of inhaled oxygen was kept less than 50%, and protective laser glasses were worn by all operative personnel.

Operative management included an initial fiberoptic bronchoscopy, performed under local anesthesia, to be sure the patient was suitable for Nd:YAG laser therapy. After the bronchoscopic assessment, general anesthesia was induced, and laser bronchoscopy was performed.

Operative management with the Nd:YAG laser consisted of initial induction of general anesthesia, followed by introduction of a rigid No. 9 ventilating Jackson bronchoscope or a Wolfe-Dumon laserscope, depending on the exact location of the lesion. An Olympus fiberoptic bronchoscope was passed through the rigid scope. Laser therapy was performed at a power density of 40 W and a pulse width of 0.5 seconds in all patients. The coagulation mode of the laser was predominantly used. After coagulation of the tumor blood supply, the majority of the tumor was quickly removed with the large biopsy forceps of the rigid endoscopic system. Any residual tumor or bleeding was touched up using the coagulation mode of the laser.

Brachytherapy

Indications for brachytherapy in 88 patients included nonresectable lesions; symptomatic lesions with an obstructed bronchus, hemoptysis, or intractable cough; and impossibility of use of conventional therapy. The 88 patients underwent a total of 230 brachytherapy treatments. Twenty-one of these patients underwent Nd:YAG laser therapy by the previously described protocol. In 18, the laser procedure was performed 2 days to 2 weeks before endobronchial brachytherapy, and in 3, laser therapy was carried out after initial brachytherapy. Of the 88 patients undergoing brachytherapy, 81 had primary bronchogenic carcinoma and 7, metastatic endobronchial carcinoma.

All endobronchial brachytherapy was performed with a Nucletron Selectron high-dose radiation remote afterloading unit using an iridium 192 source. The Selectron system is a three-channel, high-dose rate, remote afterloading system. It consists of a treatment unit, which stores the sources within a lead-shielded safe in a desktop control unit. The unit has a memory for 100 standard source loadings with the treatment times. These are automatically corrected for source decay. The treatment time and the number and positions of sources can be programmed independently for each channel to give the required dose distribution for a particular patient or tumor geometry. The accuracy of source positioning is to within ± 1 mm. The radiation source used in all patients was an iridium 192 source. The iridium 192 source is placed through a 5F catheter. Definitive or palliative radiation therapy, in doses ranging from 30 to 60 Gy (3,000 to 6,000 rads), had been given previously or was given concurrently in all but 1 patient.

Catheter placement for endobronchial brachytherapy was performed in the bronchoscopy suite with the patient under sedation and with a topical anesthetic. All procedures were performed on an outpatient basis. A 5F afterloading catheter was advanced through the working channel of the bronchoscope into the desired location, and the bronchoscope was withdrawn over the catheter. The catheter was secured at the nasal orifice, and the patient was transferred to the radiation suite. A dummy source was placed in the length of the catheter to be loaded, the determination based on chest roentgenograms and bronchoscopic findings. An iridium 192 line source was placed in the desired length of the catheter. Dosimetry consisted of a dose of 10 Gy (1,000 rads) in one fraction 1 cm from the source in all patients. Total time for delivery of this dose ranged from 10 to 14 minutes, depending on the source strength and the length of the oscillation. After completion of brachytherapy, the afterloading catheter was removed, and the patient was observed for 30 minutes and discharged. Location of catheter placement depended on the exact location of the tumor, and in this series involved the trachea, main bronchi, or lobar orifices in all patients. No subsegmental orifices were considered suitable for endobronchial brachytherapy. Each patient underwent three brachytherapy treatments at 2-week intervals, for a total of 30 Gy (3,000 rads) delivered over 4 weeks to the primary treatment area.

Results

The predominant mode of evaluation in this series was clinical evaluation combined with chest roentgenographic assessment and endobronchial reevaluation of all patients. No standard classification has been published for series comparisons of the results of therapy with the Nd:YAG laser or brachytherapy. To try to reach some degree of comparison with reported series, we attempted to classify our results with Nd:YAG laser therapy according to the classification system reported by Unger [6] and the results of brachytherapy with the classification reported by Kohek and colleagues [7]. Classification of results with Nd:YAG laser therapy is as follows:

- Excellent: restoration of tracheal or bronchial lumen, corresponding to improvement of objective variables and clinical status
- Fair: partial restoration of the lumen, correlating with some amelioration of objective variables
- Poor: no restoration of lumen and only temporary control of hemoptysis

Classification of results with brachytherapy is as follows:

- Excellent: more than 80% of normal lumen reopened
- Good: more than 50% of normal lumen reopened (minimal residual tumor)
- Fair: less than 50% of normal lumen reopened (gross residual tumor)
- Poor: no response

In both classification systems, an excellent result is associated with reopening of more than 80% of the normal lumen, with corresponding improvement in objective variables and clinical status. A good result is associated with reopening of more than 50% of the normal lumen, with some improvement in clinical symptomatology and corresponding variables. A fair result is associated with reopening of less than 50% of the bronchial lumen and the presence of major clinical symptoms. A poor result in both categories is associated with no response to the therapy.

Group 1

Group 1 (n = 130 patients) underwent Nd:YAG laser therapy only. For each patient, laser therapy was performed at a single sitting with an average of 3,750 J per patient. Each procedure required an average of approximately 32 minutes of operating time and was performed as previously described. All patients had received prior or received concomitant external-beam irradiation. All but 5 patients were treated for obstruction of the trachea, main bronchi, or lobar bronchi. Five patients were treated for hemoptysis. Following the recommendations of Dumon [3], no lesion in the left upper lobe bronchus was considered suitable for laser therapy.

Ninety-six patients had an excellent result, 24 had a good result, and 10 had a poor result. Improvement in symptoms of respiratory obstruction, including substantial improvement in shortness of breath and decrease in cough, was noted in all patients except those who had a poor result. There were three late hospital deaths. One hundred twenty-seven patients were discharged from the hospital an average of 72 hours after laser therapy. In the last year, almost all patients were discharged within 24 hours after laser therapy.

There were three complications in this group. Major bleeding developed in 1 patient approximately 3 weeks after laser therapy. The patient ultimately died and was included as a hospital death. One patient sustained an esophageal perforation. It was recognized in the recovery room, and the patient subsequently underwent surgical repair but died 6 weeks later in the hospital of respiratory distress. Another patient underwent laser therapy while on a ventilator for a high-grade obstructing lesion but was never able to be weaned from the ventilator and died 7 weeks after laser therapy, even though the airway had been cleared of the endobronchial obstruction.

Table 1. Survival of Patients Undergoing Treatment

Treatment	No. of Patients	2 Months	6 Months	1 Year
Nd:YAG	130	127	110	83
EB	67	66	60	. . .
Nd:YAG + EB	21	21	20	. . .

EB = endobronchial brachytherapy; Nd:YAG = neodymium:yttrium-aluminum garnet laser therapy.

In this group of 130 patients, 127 patients survived at least 2 months; 110 patients have survived longer than 6 months; and 83 patients have survived at least 1 year (Table 1). Eighteen patients have survived up to 2 years after laser therapy.

Group 2

Group 2 (n = 67 patients) received endobronchial brachytherapy alone. The predominant indications for therapy in this group were extrinsic bronchial compression rendering Nd:YAG laser therapy inappropriate and an obstructing lobar lesion, which made laser therapy not advisable because of proximity to major blood vessels. A total of 180 treatments were performed in these 67 patients. Each brachytherapy treatment was delivered with the Selectron high-dose afterloading unit using an iridium 192 source. Average time of treatment was approximately 12 minutes.

Of these 67 patients, 50 achieved an excellent result, 12 had a good result, and 5 received a poor result. There was 1 death; the patient sustained a massive hemorrhage at home 5 days after the third brachytherapy treatment.

In follow-up, 66 of the 67 patients survived at least 2 months, and 60 have survived 6 months or longer (see Table 1). At present, 31 patients are alive 1 year after the initial brachytherapy. The reason that there is such a large number of survivors at 1 year after brachytherapy is that we are now using it in the initial management of all patients with inoperable bronchogenic carcinoma.

Group 3

Group 3 (n = 21 patients) underwent Nd:YAG laser therapy combined with endobronchial brachytherapy. In 18 of these patients, laser therapy was performed before endobronchial brachytherapy. This group represents patients who were seen over the last 12 months of the study and who received our initial therapy for inoperable bronchogenic carcinoma with obstructive lesions in the major tracheobronchial tree. We begin all therapy with the

Nd:YAG laser or endobronchial brachytherapy or a combination in appropriate patients. All of these patients had major obstruction to the trachea or main bronchi, and the symptomatology was predominantly shortness of breath, with minor bleeding in 2 patients. Each patient received a total of three endobronchial brachytherapy treatments with 10 Gy (1,000 rads) delivered at 1 cm on each treatment, and a total of 30 Gy (3,000 rads) delivered over 1 month.

Nineteen patients had an excellent result, and 2 patients had a good result; no patient had a poor result. There were no deaths in this group.

All 21 patients have survived at least 2 months (see Table 1). Twenty patients have survived 6 months or longer. Follow-up beyond 6 months is incomplete.

Among the 88 patients who underwent brachytherapy (groups 2 and 3), 4 experienced complications. One patient had minor bleeding, which subsequently subsided, after the procedure. Another patient complained of marked shortness of breath, which led to hospitalization. Two patients had major chest pain, which was relieved by partial withdrawal of the catheter.

Comment

When non–small cell bronchogenic carcinoma is initially unresectable, is medically inoperable, or represents recurrent disease after resection, previous methods of therapy, whether palliative or with curative intent, have consisted of external-beam irradiation, combination chemotherapy, or both. Local recurrence with symptomatic airway obstruction is common after initial definitive therapy or develops after previous chemotherapy, radiation therapy, or both. In recent years, it has been suggested [8–11] that Nd:YAG laser therapy and endobronchial brachytherapy have the potential to prove major palliation in the management of inoperable bronchogenic carcinoma.

During the past 2 years, if a patient is considered to have initially inoperable bronchogenic carcinoma on the basis of physiological, anatomical, or medical reasons, we have used Nd:YAG laser therapy, endobronchial brachytherapy, or a combination of these as part of our initial management. After initial laser therapy or endobronchial brachytherapy, external-beam irradiation is added concurrently as is combination chemotherapy, when appropriate. During the past year, we have entered into trial protocols combining Nd:YAG laser therapy, external-beam irradiation radiotherapy, brachytherapy, and adjunctive chemotherapy with VP-16, *cis*-platinum, and Velban (vinblastine sulfate).

Laser therapy presents a means to immediately reopen occluded bronchi. The results when the trachea or main bronchi are occluded with a high-grade occlusion are quite dramatic. Immediate improvement in pulmonary function studies, arterial blood gases, and chest roentgenograms is very evident. In the past 2 years, we have refined our laser technique to include a short operating time with coagulation of the tumor blood supply and immediate removal of all bulk tumor with the large biting forceps. This has reduced our intraoperative time to approximately 30 to 45 minutes in all patients. All laser procedures are done at a single sitting, and we have not performed staged laser intervention in the past 4 years.

The term *brachytherapy* refers to that form of radiotherapy with a short distance between the radiation source and the target area [12]. The principal use has been to deliver a high-dose treatment to a small target volume. Brachytherapy is useful in exophytic endobronchial disease and extrinsic endobronchial disease. One advantage of brachytherapy is the ability to deliver high intensities of radiation to a controlled position without damage to external tissues. Patient comfort and safety factors are easy to control, and the accuracy of dosimetry is extremely precise. There have been minimal complication rates and very excellent response rates. The potential complications of brachytherapy include increase in symptomatology of shortness of breath, bronchial necrosis, bleeding, fistula formation, and arrhythmias. In our observation of more than 230 treatments, we have not noted any of these to be a major problem.

Endobronchial brachytherapy can be used concurrently with or after maximum external radiotherapy without any major radiation consequences.

Historically, Sidney Yankauer presented his experience with brachytherapy on June 1, 1921, to the American Bronchoscopic Society in New York [13]. In 1961, Poole [14] reported his experience with 42 patients in whom a radon-containing capsule was inserted through a rigid bronchoscopic system. In 1978, Hilaris and Martini [15] published their experience with interstitial brachytherapy in a large number of patients. Five years later, Mendiondo and associates [16] reported the successful utilization of a rigid bronchoscope with implantation of a radionuclide. They also reported the utilization of a fiberoptic bronchoscope with placement of a small polyethylene tube into a bronchus through which an iridium 192 seed was implanted. In 1985, Schrady and others [12] observed that the response to the Nd:YAG laser lasted longer when followed with brachytherapy. Despite decades of favorable experience with endobronchial brachytherapy for recurrent malignant airway obstruction, its use has been limited to a few institutions and a small number of patients. Possible reasons for this include the following: considerable technical skill and special equipment are required; the procedure is associated with potential risk; considerable technical support is required; and radiation therapy is a concern [8].

One of the major advantages of endobronchial brachytherapy is the ability to place a radioactive source near the tumor area. The high-dose radiation content is given to the tumor, but the dose falls off rapidly because of the inverse square law. As only a small volume of tissue receives a normal therapeutic dose of radiation, the chance of severe normal tissue damage is markedly reduced [8, 9]. Consequently, brachytherapy is being used for repeat irradiation in multiple sites with an acceptably low complication rate.

The dosimetry of 10 Gy (1,000 rads) at 1 cm can potentially be criticized. However, in our hands, this dose

Table 2. Survival and Improvement

Reference	Type of Treatment[a]	Survival: Mean (d)	Survival: Longest (d)	Improvement (%)
Unger[b]	None (control)	200	220	. . .
	Nd:YAG	400	565	. . .
Speiser and Spratling [17]	EB (45)	220	365 (28%)	65
Kohek et al [7]	Nd:YAG + EB (15)	161	16 mo (37%)	. . .
Schrady [18]	EB (40)	. . .	. . .	60
	Nd:YAG + EB (61)	. . .	. . .	64
Miller and Phillips [present study]	EB (67)	. . .	120	70
	Nd:YAG + EB (21)	. . .	120	. . .
	Nd:YAG (130)	460	600	80

[a] Numbers in parentheses are numbers of patients. [b] This was a personal communication, 1989.

EB = endobronchial brachytherapy; Nd:YAG = neodymium:yttrium-aluminum garnet laser therapy.

has worked well, providing acceptable results with a low complication rate.

Part of the problem in trying to quantify results is due to the fact that there are few centers reporting experience with this combined modality therapy and the fact that there are no standard criteria for defining good and excellent results with these modalities.

In an attempt to quantitate survival and improvement with other reported series, we compiled Table 2. Unger found that for 1,000 patients receiving Nd:YAG laser therapy, the mean survival was 400 days and the longest survival, 565 days (M. Unger, personal communication, 1989). Speiser and Spratling [17] reported that of 45 patients who underwent endobronchial brachytherapy, 28% survived at least 12 months. They also noticed an overall improvement rate of 65%. Kohek and co-workers [7] presented their results in 15 patients who underwent combined Nd:YAG laser and endobronchial brachytherapy. The mean survival was 161 days, and 37% of patients survived up to 16 months.

From the Mayo Clinic, Schrady [18] reported that 60% of 40 patients who underwent endobronchial brachytherapy showed noted improvement. In an additional 61 patients who underwent combined Nd:YAG laser therapy plus endobronchial brachytherapy, 64% showed improvement. Schrady and associates [8] believe that brachytherapy appeared to have prolonged the duration of palliation by laser therapy in the majority of patients by a factor of two to three times based on a retrospective review of their laser experience. Because of this information, they believe that brachytherapy is a valuable adjunct to laser therapy in the treatment of inoperable carcinoma.

In our series of patients, the longest survival of a patient undergoing endobronchial brachytherapy has been more than 1 year. For the 21 patients who underwent combined Nd:YAG laser therapy and endobronchial brachytherapy, the longest survival has been 120 days. For the 130 patients who underwent Nd:YAG laser therapy, the mean survival has been 460 days and the longest survival, 600 days. More than 80% of the patients who underwent Nd:YAG laser therapy have reported a good to excellent result.

Based on our results in this study, we believe that the following are reasonable considerations in the management of inoperable initial or recurrent non–small cell bronchogenic carcinoma:

1. For inoperable or unresectable non–small cell bronchogenic carcinoma with proximal, endobronchial, or tracheal exophytic disease, we begin with Nd:YAG laser therapy followed in 48 to 72 hours by endobronchial brachytherapy. This is subsequently followed with external-beam radiation therapy and, in appropriate instances, ie, if the patient is considered suitable, with combination chemotherapy.
2. For inoperative or unresectable non–small cell bronchogenic carcinoma with proximal endobronchial extrinsic compressive disease, we begin with endobronchial brachytherapy followed by external-beam radiotherapy.

We think that the use of Nd:YAG laser therapy and endobronchial brachytherapy improves the quality of survival in more than 80% of patients. It also appears to enhance a longer period of survival.

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DISCUSSION

DR HARVEY I. PASS (Bethesda, MD): This is a beautiful series. I just have a couple of specific questions. When do you do your first follow-up bronchoscopy after treatment?

DR MILLER: The follow-up bronchoscopy is done 1 month after laser therapy and 1 month after endobronchial brachytherapy at no cost to the patient.

DR PASS: My other question concerns the subgroup of patients who may benefit most from this treatment, ie, the patients who have failed conventional treatment, which means they have had radiation therapy. Some reports indicate that you can gauge whether these patients are going to respond to endobronchial brachytherapy by the previous response to irradiation. Have you found that to be the case?

DR MILLER: In the early part of the series, the majority of these patients had all initially undergone conventional radiation therapy previously. In the last 2 years, we have used this as part of our initial approach in the management of all these patients. Endobronchial brachytherapy has the advantage in that you can take a localized area that has already received 55 to 65 Gy (5,500 to 6,500 rads) and deliver 30 Gy (3,000 rads) directly to it and achieve substantial improvement. For instance, if you have an obstructing right upper lobe lesion that has previously been irradiated, you can come back and irradiate it either for obstructive reasons or for bleeding and get very good results.

DR THOMAS M. DANIEL (Charlottesville, VA): I am delighted to see thoracic surgeons playing an aggressive role in this area. My question has to do with patient selection. We all know that proximal tracheobronchial and main bronchial lesions respond very dramatically. However, in the case of lobar lesions, particularly when brachytherapy is used, I question whether the area you are opening up for ventilation is perfused, because we see many tumors at operation in which the arterial supply or the venous supply is interrupted. How do you select lesions and know that you are reventilating an area that has functional lung tissue in those peripheral lesions?

DR MILLER: I will answer your question as best I can. It is an objective assessment based predominantly on endoscopic observation. We have not obtained ventilation/perfusion lung scans for endobronchial brachytherapy in a patient with an isolated lobar lesion, for example, which is predominantly where these scans have been used. At initial therapy, we base the opening up on chest roentgenographic reassessment after therapy and also on endoscopic observation. We really have not done anything to check perfusion of that area by ventilation/perfusion scans either before or after therapy.

DR KAMAL A. MANSOUR (Atlanta, GA): I compliment my colleague and associate, Dr Miller, for taking on himself such an ethical dilemma as the care of morbid cancer patients for whom the goal of therapy is short-term palliation and not cure. I have, however, a word of caution regarding primary malignant lesions of the lower trachea, the main bronchi, and the lobar bronchi. For these, bronchoplastic procedures and sleeve resections offer far more superior results than laser and intraluminal brachytherapy.

I have two questions. First, what do you do for lesions totally obstructing and extrinsically occluding or compressing the airway? Second, for primary tumors of the trachea or main bronchi, do you consider reevaluating these patients for possible surgical intervention or does your therapy preclude any further operative intervention?

DR MILLER: First of all, whenever surgical intervention is appropriate, we try to be aggressive and, as Dr Mansour knows, to resect anything if at all possible. All of these patients are considered to have essentially inoperable or gross anatomical disease. If there is a lesion obstructing the trachea or main bronchi in the distal third of the trachea, the airway is generally opened up with the Nd:YAG laser followed by gross bulk removal, which really is accomplished fairly easily though it is necessary to be very careful. A very good anesthesiologist is a must.

Second, endobronchial brachytherapy does not preclude coming back and doing a sleeve resection or a resection in the trachea, because you are delivering only a total of 30 Gy (3,000 rads) in the three treatments the patient is given. Endobronchial brachytherapy would not preclude resection if after adjunctive chemotherapy, for example, or reduction chemotherapy, you wanted to do it. Nor would laser therapy.

DR DAVID H. HARPOLE (Roanoke VA): My question is whether you are using the open-beam Nd:YAG laser or the contact probe? We have been using the open beam for some time, and I congratulate you on getting these patients primarily. The patients we usually see are the ones in whom radiation therapy has failed, and laser therapy is not as easy a job at that stage.

DR MILLER: We have used the open-beam laser. Part of the reason we see so many of these patients is that almost all of the people in our institution are geared toward considering brachytherapy or laser therapy. Hence, after the patients have seen the pulmonologists and after they have been deemed unsuitable candidates for operation after surgical evaluation, these patients generally are referred for one of these two types of therapy, if applicable. I emphasize that this group is a small percentage of the total number of patients seen. Even though it is a very select group, it represents only a very small percentage of the patients with bronchogenic carcinoma.

Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 16, 1992. The closing date for registration is August 1, 1991.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Reappraisal of Localized Resection for Subvalvar Aortic Stenosis

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Between June 1972 and August 1989, we operated on 45 patients with fixed subaortic stenosis. Discrete membranous stenosis was present in 28 patients and tunnel stenosis, in 13. Four patients had subvalvar stenosis complicating double-outlet right ventricle. There were 33 male and 12 female patients. Mean age at operation was 7.1 ± 4.3 years (range, 6 months to 21 years). Local resection of the fibrous membrane was performed in 26 patients. Local resection was combined with myectomy in 18 patients. Aortoventriculoplasty (modified Konno procedure) was required at operation in 3 patients. There were three perioperative deaths at initial operation and two deaths at the time of reoperation. Follow-up ranges from 1 month to 17 years (average follow-up, 47.0 months). Reoperation for recurrent obstruction has been required in 12 patients (27%), and 3 patients have required a second reoperation. Mild to moderate aortic regurgitation was present in 17 patients. Subaortic stenosis is a spectrum of anatomical derangements ranging from a discrete fibrous membrane to a long, tortuous fibrous tunnel with aortic annulus hypoplasia. Successful removal of a discrete fibrous membrane can be followed later by recurrent stenosis necessitating myectomy or aortoventriculoplasty. Correction of subvalvar aortic stenosis can be followed by recurrent stenosis necessitating reoperation as long as 17 years after the initial procedure.

(Ann Thorac Surg 1990;50:197–203)

Localized resection for fixed subvalvar aortic stenosis has been the accepted surgical approach for many years. Resection of a discrete fibrous membrane alone or in combination with septal myectomy for diffuse "tunnel" stenosis has led to acceptable early results [1–7]. Although correction of subvalvar aortic stenosis may have been considered by many a curative procedure, several series have documented high rates of recurrence [6, 8–15]. The number of reoperations we have performed on patients with recurrent subaortic stenosis stimulated us to review our experience with these lesions at Vanderbilt University over the past 17 years.

Material and Methods

The records of all patients undergoing operation for subvalvar aortic stenosis at Vanderbilt University Hospital from June 1972 through August 1989 were reviewed. Specific data collected included date of birth, date of operation, sex, associated cardiac anomalies, previous operations, and results of catheterization and echocardiographic examinations. Lesions were classified as discrete membranous or diffuse tunnel stenosis based on surgical observation. Details of the operative procedure as well as deaths and complications were recorded. Follow-up data were collected by examination and questionnaires completed by referring physicians.

Echocardiograms and catheterization studies were reviewed for the left ventricular–aortic gradient as well as the presence and severity of aortic or mitral regurgitation. Associated cardiac anomalies were documented. Patients were offered operation if aortic regurgitation or left ventricular dysfunction accompanied subvalvar stenosis, if the left ventricular–aortic gradient was progressive or severe, or if symptoms of dyspnea, fatigue, chest pain, or syncope developed with a moderate gradient. Indications for operation and reoperation were similar.

Operative Techniques

Subaortic obstruction was resected using cardiopulmonary bypass with moderate hypothermia and 4°C hyperkalemic crystalloid cardioplegia. Two patients were operated on in 1972 before the routine use of cardioplegic solution, and 2 additional patients underwent repair using hypothermia and circulatory arrest. Membranous lesions were removed from the left ventricular outflow tract (LVOT) using sharp excision. The muscular or fibrous component of tunnel stenosis was treated with myectomy or myotomy. Great care was taken to avoid damage to the mitral valve apparatus and the conduction system. When present, diffuse LVOT stenosis with aortic annulus hypoplasia was treated with a Rastan-Konno procedure with aortic valve replacement [13, 16]. Associated lesions were repaired as indicated.

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Table 1. Associated Congenital Cardiac Anomalies

Anomaly	No. of Patients[a]
Ventricular septal defect	9
Coarctation	9
Valvar aortic stenosis	8
Bicuspid aortic valve	9
Mitral stenosis	4
Supravalvar aortic stenosis	2
DORV	4
PDA	3
Incomplete AV septal defect	2
TGA	1
Infundibular pulmonary stenosis	1

[a] Of 28 patients with multiple lesions, 16 had more than one associated cardiac abnormality.

AV = atrioventricular; DORV = double-outlet right ventricle; PDA = patent ductus arteriosus; TGA = transposition of the great arteries.

Statistical Analysis

Survival data were analyzed using the Kaplan-Meier method and are presented as actuarial survival with 70% confidence limits (CL). Perioperative deaths were defined as deaths within 30 days of operation and are included in all survival statistics. Cumulative hazard function for death and reoperation was determined (BMDP Statistical Software, Inc). Actuarial incidence of reoperation is presented as percent surviving without reoperation. Left ventricular outflow gradients as determined by catheterization and echocardiography are treated interchangeably. Data are presented as the mean ± the standard deviation.

Results

Forty-five patients underwent 60 operations for fixed subvalvar aortic stenosis from June 1972 through August 1989 at Vanderbilt University Hospital. There were 33 male and 12 female patients. Mean age at operation was 7.1 ± 4.3 years (range, 6 months to 21 years). Isolated subvalvar aortic stenosis was present in 17 patients, and 28 had associated cardiac anomalies (Table 1). Twelve patients had had 17 previous operations for associated congenital cardiac anomalies. Four patients had had more than one previous operation. Associated cardiac anomalies repaired at previous operations are listed in Table 2.

Discrete membranous subaortic stenosis was encountered in 28 patients (62%), and diffuse narrowing of the ventricular outflow tract, tunnel stenosis, was found in 17 (38%), 4 of whom had double-outlet right ventricle (DORV). Resection of a discrete fibrous membrane was performed at initial operation in 26 of the 28 patients with discrete subvalvar stenosis. Two patients had limited septal myectomy in addition to resection of the discrete shelf. Of the 13 patients with tunnel stenosis, 12 had local resection of fibromuscular tissue combined with myectomy. Two patients with associated incomplete form of atrioventricular septal defect had concomitant mitral valve replacement to eliminate LVOT obstruction. Aortoventriculoplasty was performed as a primary procedure in 1 patient who had diffuse tunnel stenosis, valvar aortic stenosis with annulus hypoplasia, and supravalvar aortic stenosis.

Table 2. Associated Cardiac Anomalies Repaired at Previous Operation

Anomaly	No. of Patients[a]
VSD	4
Pulmonary artery band	2
Coarctation	7
Valvar aortic stenosis	2
Supravalvar aortic stenosis	1
Mitral stenosis	2
PDA	2
Incomplete AV septal defect	1

[a] There were 17 previous operations for associated lesions in 12 patients. Four patients had had more than one previous operation.

AV = atrioventricular; PDA = patent ductus arteriosus; VSD = ventricular septal defect.

Fourteen patients had associated lesions repaired at operation for subvalvar aortic stenosis; 4 of them had more than one lesion repaired concomitantly (Table 3).

Reoperation

Reoperation was required for recurrent subvalvar aortic stenosis in 12 patients (12/45, 27%), including the 4 with DORV. Five patients (5/28, 18%) initially seen with a discrete membranous stenosis and 3 patients (3/13, 23%) seen initially with diffuse narrowing of the subvalvar area had recurrent obstruction necessitating reoperation. Two

Table 3. Operations Performed Concurrently With Repair of Subaortic Stenosis

Operation	No. of Patients[a]
VSD repair	6
Aortic valvotomy	2
Coarctation repair	1
Ligation of PDA	1
Aortic valve replacement	1
Konno	1
Repair of supravalvar aortic stenosis	2
Mitral valve replacement	2
Mitral valvotomy	1
Resection of infundibular pulmonary stenosis	1

[a] Fourteen patients had associated lesions repaired at operation for subvalvar aortic stenosis. Four patients had more than one associated lesion repaired.

PDA = patent ductus arteriosus; VSD = ventricular septal defect.

Table 4. Reoperations

Disease Process	No. of Patients[a]	Type of Reoperation
First reoperation		
Discrete stenosis	5	Reexcision of membrane, 2*; excision and myectomy, 3
Tunnel stenosis	3	Modified Konno, 2; AVR, Manouguian, myectomy, 1
DORV	4	Septal myectomy, 3; patch revision and membrane excision, 1*
Second reoperation		
Discrete stenosis	2	Excision and myectomy, 2
DORV	1	Septal myectomy, 1

[a] There were 15 reoperations in 12 patients.

AVR = aortic valve replacement; DORV = double-outlet right ventricle; * = second reoperation necessary.

of the 3 patients with tunnel stenosis required aortoventriculoplasty at reoperation to relieve multilevel LVOT obstruction. The other patient, who had refused earlier reoperation, required enlargement of the LVOT using a Rittenhouse-Manouguian patch [17, 18], aortic valve replacement, and septal myectomy.

Three patients (3/12, 25%) required a second reoperation. One patient who had had patch revision and membrane excision for subvalvar stenosis after repair of DORV required reoperation with septal myectomy to relieve diffuse subvalvar stenosis. The other 2 patients were seen initially with a discrete membranous stenosis and had had simple membrane excision at first operation. Recurrent stenosis developed that was treated by reexcision of a discrete shelf. In both, a second, more diffuse fibromuscular stenosis developed, necessitating septal myectomy 16 and 17 years after the initial operation. Details of reoperations are presented in Table 4.

Age at initial operation for the patients with recurrence (6.3 ± 3.3 years) does not differ significantly from that of the group as a whole (7.1 ± 4.3 years) or those in whom restenosis did not develop (7.5 ± 4.5 years).

Risk of need for reoperation increased with time postoperatively (Fig 1). Eighty-five percent of patients (CL, 93% to 77%) are free from reoperation at 5 years, 36% (CL, 51% to 21%) at 10 years, and 24% (CL, 38% to 10%) at 15 years. Cumulative hazard function for reoperation is presented in Figure 2 and demonstrates an increased cumulative risk with time postoperatively.

Survival Data

Three patients died perioperatively after initial operation for subvalvar aortic stenosis (6.7% mortality rate). One patient had a stenotic membrane at the orifice of the left coronary artery and died of left ventricular failure in the first postoperative day. Another patient with valvar and subvalvar aortic stenosis and DORV had had previous closure of an outlet ventricular septal defect and died 3 years later at the time of repair of subvalvar aortic stenosis. At postmortem examination, the patient was found to have supravalvar mitral stenosis. One patient had diffuse tunnel stenosis in addition to valvar and supravalvar stenosis, and died of low cardiac output 1 day after a modified Konno operation. Perioperative mortality data are presented in Table 5.

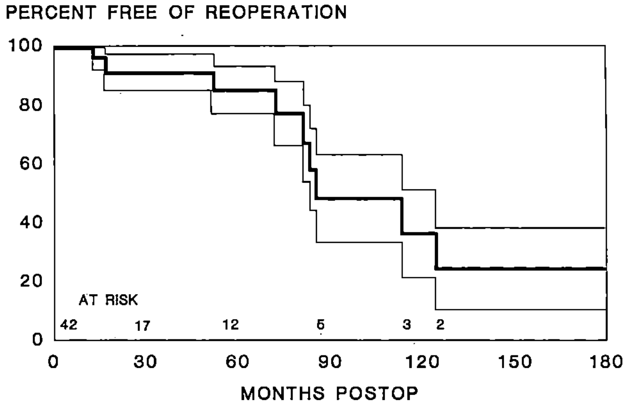

Fig 1. Actuarial incidence of freedom from reoperation after initial operation for subvalvar aortic stenosis. Data are presented with 70% confidence limits.

There were 2 perioperative deaths (2/15, 13%) at the time of reoperation. One patient died after aortoventriculoplasty 13 months after the initial operation at another institution. Two previous procedures were mitral and aortic valvotomies with resection of subaortic membrane and supraannular mitral valve replacement. At postmortem examination, there was pannus ingrowth into the mitral prosthesis with entrapment of the posterior leaflet, which led to mitral stenosis. The other postoperative death at reoperation occurred in a poorly compliant patient who refused reoperation after an episode of aortic endocarditis and was seen for reoperation 17 years after the initial procedure with severe biventricular failure. Excision of recurrent membrane and septal myectomy as well as aortic valve replacement with annulus enlargement was performed. The patient experienced ventricular

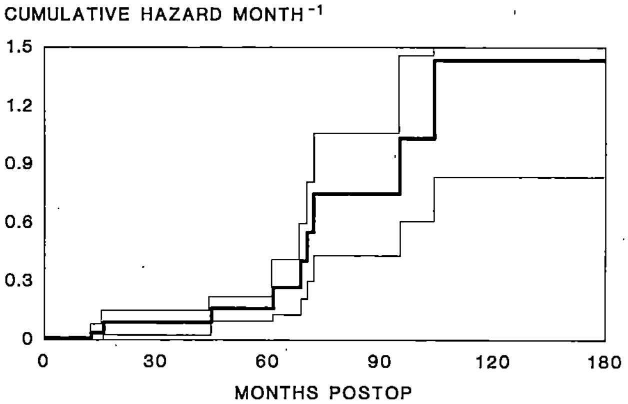

Fig 2. Cumulative hazard function for reoperation. Data are presented with 70% confidence limits.

Table 5. Perioperative Mortality[a]

Diagnosis/Operation	No. of Patients	Deaths
Initial Operation		
Discrete	28	2 (7.1)
Membrane excision	26	2 (7.7)
Excision + myectomy	2	0
Tunnel	13	1 (7.7)
Excision + myectomy	12	0
Konno	1	1 (100)
DORV	4	0
Total	45	3 (6.7)
Reoperation		
Discrete	7	0
Reexcision	2	0
Reexcision + myectomy	5	0
Tunnel	3	2 (67)
Konno	2	1 (50)
Manouguian	1	1 (100)
DORV	5	0
Myectomy	5	0
Total	15	2 (13.3)

[a] Numbers in parentheses are percentages.
DORV = double-outlet right ventricle.

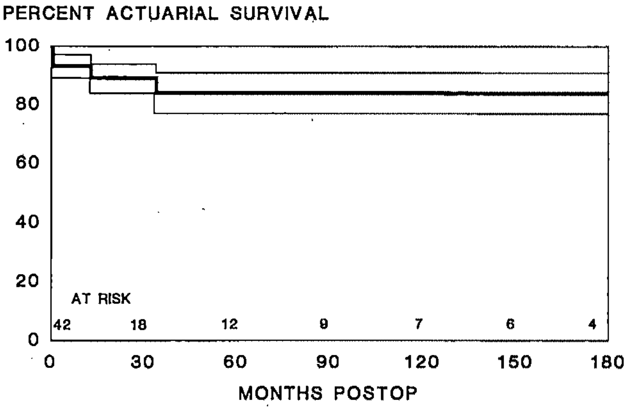

Fig 3. Actuarial survival, including hospital mortality, of patients operated on for fixed subvalvar aortic stenosis. Data are presented with 70% confidence limits.

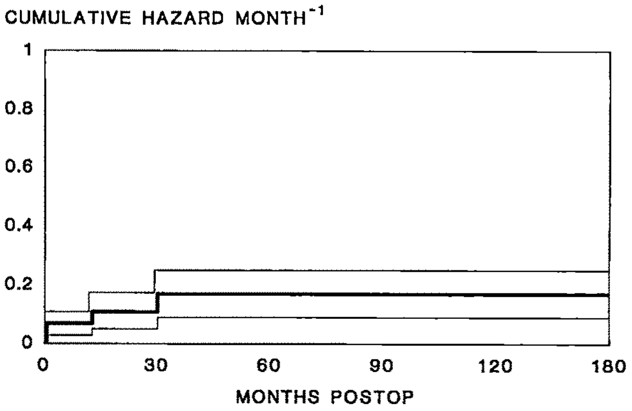

Fig 4. Cumulative hazard function for death. Data are presented with 70% confidence limits.

fibrillation postoperatively, and the heart could not be defibrillated.

Actuarial survival is 93% (CL, 97 to 89) at 1 year and 84% (CL, 91 to 77) at 5, 10, and 15 years (Fig 3). Follow-up beyond 203 months exceeds the 95% CL for median survival and assumes no significance. Follow-up ranges from 2 months to 17 years (average follow-up, 47.0 months). Cumulative hazard function for death is presented in Figure 4, and remains stable during the follow-up to 203 months.

Hemodynamic Results

Data regarding the left ventricular–aortic gradient were available for 43 patients preoperatively, 39 patients within the first month postoperatively, and 26 patients late postoperatively. For the group, left ventricular outflow gradient decreased from a mean value of 79 ± 31 mm Hg preoperatively to 22 ± 23 mm Hg immediately postoperatively (Table 6). Patients with tunnel stenosis had a mean gradient of 82 ± 36 mm Hg preoperatively compared with 95 ± 24 mm Hg for those with subvalvar stenosis complicating DORV and 75 ± 30 mm Hg for those with discrete stenosis. Although satisfactory relief of LVOT obstruction has been achieved in most patients late postoperatively, there are 4 patients with gradients in excess of 30 mm Hg. Three patients with discrete stenosis have residual gradients of 44, 57, and 58 mm Hg. One patient who had a

Table 6. Left Ventricular–Aortic Gradient[a]

	Preoperative		Early Postoperative		Late	
Patient Group	No. of Patients	Gradient	No. of Patients	Gradient	No. of Patients	Gradient
All	43	79 ± 31	39	22 ± 23	26	17 ± 17
Discrete	27	75 ± 30	26	19 ± 21	17	19 ± 19
Tunnel	12	82 ± 36	11	30 ± 28	7	12 ± 12
DORV	4	95 ± 24	2	50 ± 42	2	28 ± 11

[a] Gradient data are shown as the mean ± the standard deviation in millimeters of mercury.
DORV = double-outlet right ventricle.

gradient of 120 mm Hg and DORV had a residual gradient of 80 mm Hg after resection and patch revision, and now has a 36 mm Hg gradient after reoperation.

Aortic regurgitation was evaluated preoperatively and postoperatively in all patients. Fourteen patients had mild aortic regurgitation preoperatively and 3, moderate aortic regurgitation. Regurgitation resolved after operation in 3 patients, in 1 of whom it was moderate preoperatively. Aortic regurgitation progressed from mild to moderate early postoperatively in 2 patients. New mild aortic regurgitation developed postoperatively in only 1 patient. With late follow-up, regurgitation progressed from mild to moderate in 2 patients, 1 of whom was treated for endocarditis. There was no trend for aortic regurgitation to increase perioperatively, nor did it appear to increase during the period of follow-up in the absence of endocarditis.

Arrhythmias were seen in 4 patients. Two patients required pacemaker insertion for late postoperative heart block. Transient junctional ectopic tachycardia was observed in 1 patient, and another patient had persistent premature ventricular complexes postoperatively.

Comment

Results of surgical treatment of fixed subvalvar aortic stenosis over the past 29 years indicate that most patients show improvement after localized resection and are long-term survivors [1–15, 19, 20]. As follow-up increases, however, there is evidence that recurrent stenosis becomes a real threat to survival.

In our series, the need for reoperation increased with time postoperatively (see Figs 1, 2). Both patients with discrete stenosis and patients with tunnel stenosis are at risk. Isolated discrete subvalvar aortic stenosis is not observed in neonates. A strong case can be made, therefore, that this is an acquired condition [15]. Its pathogenesis possibly is related to an abnormality in the contraction pattern of the left ventricle, creating turbulence in the LVOT, or to an abnormality in the relationship of the subaortic LVOT to the mitral valve. We hypothesize that the cause of recurrent stenosis is related to scar formation in the subvalvar area as it heals, thus fixing the size of the LVOT. With growth, a fixed outflow tract results in recurrent stenosis in the absence of further narrowing. The development of localized hypertrophy and fibrosis can result in fibromuscular recurrence even though the initial lesion was a discrete membrane. Limited myectomy is performed in addition to local resection of the discrete membrane if the LVOT remains narrowed after membrane excision, in the hope of preventing or at least delaying the onset of recurrent stenosis. More liberal use of aortoventriculoplasty for patients with severe tunnel or multilevel aortic stenosis might improve recurrence rates in these patients.

Fixed subvalvar aortic stenosis is frequently associated with other congenital cardiac anomalies that require separate or simultaneous correction. Aortic regurgitation tends to remain mild to moderate if present preoperatively, and it worsens substantially postoperatively if endocarditis or recurrent stenosis develops.

Given the possibility of recurrent subvalvar aortic stenosis, we recommend diligent postoperative follow-up with surveillance echocardiography. Recently, other authors [20] recommended early operation for patients with fixed subvalvar aortic stenosis. On the basis of our data, we recommend operation (and reoperation) if aortic regurgitation or left ventricular dysfunction is present, if the left ventricular–aortic gradient is progressing or severe, or if there are symptoms of dyspnea, fatigue, chest pain, or syncope in the presence of a moderate gradient. Late mortality after a successful initial operation in our series was not associated with progressive aortic regurgitation or endocarditis, but was related to the need for and performance of reoperation.

We acknowledge the assistance of John A. Carey, FRCS(I), with manuscript preparation and statistical analysis.

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DISCUSSION

DR ROBERT M. SADE (Charleston, SC): Dr Stewart, do I interpret your actuarial curves correctly as depicting that recurrence will eventually develop in virtually all patients? If that is the case, what is the level of statistical confidence that this observation is true?

DR ROBERT A. GUSTAFSON (Morgantown, WV): I enjoyed your presentation very much. I have several questions. Can you better define your original indication for primary operation, ie, are you operating on a particular gradient or are you waiting until there is some aortic insufficiency? Would you operate on a 3-year-old patient with a gradient of 25 mm Hg and no aortic insufficiency? What are your criteria for deciding when to reoperate? Can you say from your data if we should perform a myectomy at the initial operation for a discrete isolated subaortic membrane?

DR DAVID R. CLARKE (Denver, CO): I enjoyed your paper very much, Dr Stewart. I have a comment and two questions for you. A number of years ago, my colleagues and I reviewed a series of patients with discrete subvalvar aortic stenosis who had a myectomy at the initial procedure. The recurrence rate in this group was 20%, which is somewhat less than the incidence you presented. In those patients who did have recurrence, if they underwent another direct resection, the re-recurrence rate within 5 years was approximately 80%.

Now for my questions. First, in your series, was the performance of a myectomy at the original operation in any way related to the risk of recurrence? Second, did you attempt to use β-blocker therapy in any patient to prevent recurrence? In our experience, such therapy is frequently effective in reducing the immediate postoperative gradient, but it does not prevent recurrence in the long term.

DR MILTON V. DAVIS (Kaufman, TX): I have just one question. Is it correct that there was no heart block in your series?

DR SADE: I have one more comment to add. There are more risks than the risk of recurrence after operation for these patients. They are at risk for the development of aortic insufficiency, and they are at risk for the development of infective endocarditis; not operating may carry a higher risk than operating. My concern is whether your criteria for operation are too stringent; perhaps we should be operating on these children earlier than you are suggesting.

In subvalvar aortic stenosis, the incidence of aortic insufficiency is higher in older patients, ie, there may be progression of aortic insufficiency in patients who do not undergo operation. Within 10 years after operation, new aortic insufficiency may appear in 15% of these patients. Aortic insufficiency is not related to the severity of the LVOT gradient.

The incidence of endocarditis is 12% to 25% in these patients who do not have surgical intervention. That is fully ten times greater than any other congenital heart malformation. Infective endocarditis is associated with aortic insufficiency, which develops in patients who do not have operation, as well as the presence of a high gradient. It is rare after operation if a low gradient is achieved and there are no residual anatomical lesions.

When my colleagues and I reviewed our series recently, we concluded based on observations from our own series and from pertinent literature, that although there are no clear answers to the question of when subaortic stenosis should be resected, the weight of the evidence suggests that it is reasonable for a patient with subaortic stenosis to undergo operation at the time the diagnosis is made rather than wait for specific and arbitrary indications, as described in this presentation.

DR STEWART: Dr Sade, I am very confident that there is a significant recurrence rate in patients with discrete subvalvar aortic stenosis. The data are presented here with one standard deviation, and I think they are very solid out to 203 months. There is no question that there is a high risk of recurrence over a period of about 15 years in patients with discrete stenosis, and I think we have hypothesized as to how that develops.

Dr Gustafson, concerning operative indications, the age of the patients we operated on is much younger than in most series. The average age in our series was only 7 years, and this includes the adults. In the past we have had relatively liberal operative criteria. A gradient greater than 50 mm Hg or symptoms, progressive hypertrophy, evidence of left ventricular dysfunction, or regurgitation led us to operate. Even with this liberal policy, we have seen a large number of recurrences. Perhaps the younger the patients at the time of operation, the more recurrences we are going to see, because we are fixing the size of the aortic outflow at the time of initial resection.

When do we reoperate? Our reoperative indications are very similar to our operative indications. If the patient has a progressive or severe gradient, again with aortic regurgitation or left ventricular dysfunction, we reoperate.

Should we do a myectomy on all patients with discrete membranous stenosis? I think if the membrane has been excised and the LVOT looks absolutely normal, it is a little dangerous to do something that may not be indicated. The patient may be 1 of those 25% of patients who is going to make it to 15 or 20 years and not need reoperation. However, we do add a myectomy whenever there is some evidence of narrowing of the outflow tract after we have completely excised the membrane.

Dr Clarke, in our series, the performance of myectomy at initial operation was not a risk factor for recurrence. Supposing, however, that myectomy is performed more commonly in patients with tunnel or multilevel LVOT stenosis, it would appear to make sense that residual stenosis as well as recurrence would be a problem and lead to a large number of reoperations.

As far as β-blockers are concerned, I think that they are very helpful for patients who have a dynamic stenosis in the LVOT, and by giving β-blockers, you can diminish the contractility and therefore the gradient. However, we believe the size of the outflow tract becomes fixed after resection and will not be affected by the use of β-blockers.

Dr Davis, we had 1 patient with heart block and 1 patient with difficult atrial arrhythmias postoperatively who required pacemaker insertion for management. These are the only 2 patients in whom a pacemaker was necessary.

As far as aortic regurgitation is concerned, Dr Sade, I know about your data, but in our series, aortic regurgitation did not increase with time postoperatively. We will stick by our guns and operate on the patients for the indications that we have stated. Although we did have 1 patient in whom endocarditis developed postoperatively, risk of death in our patients was clearly associated with reoperation.

REVIEW OF RECENT BOOKS

Transplant—A Heart Surgeon's Account of the Life-and-Death Dramas of the New Medicine

By William H. Frist, MD
New York, Atlantic Monthly Press, 1989
267 pp, $18.95

Reviewed by Benson B. Roe, MD

This lucid and informative narrative addresses a fascinating subject that has evoked massive publicity and consequent public interest. The reader is treated to an easy-to-read authoritative overview of transplantation history and ongoing development through the eyes of a young, vigorous, and thoughtful surgeon as he faces the challenges of starting a new program.

The young Dr Frist has a storybook background from which he projects a flavor of how things "should be." His father is a conscientious, "straight arrow," successful, and beloved physician-turned corporate executive. The author obtained his medical education and residency training in leading institutions and topped off this superb grounding with an apprenticeship under Norman Shumway at Stanford's pioneering and world-leading center of heart transplantation.

Doctor Frist avoids aggrandizing his important accomplishments and successfully evokes empathy as he provides the reader with a vivid feeling of the drama, the stress, the problems, the frustrations, and the disappointments of his work on the cutting edge of medical science. He carries the reader through the complex logistics and mechanics of procuring the donor heart with their attendant impact on both the involved individuals and their families. He weaves fascination into his role of orchestrating the psychological impact of the transplantation drama on both donor and recipient, as well as on the personnel of the transplant team.

It is difficult for me to examine the scenario dispassionately because it contains so much deja vu for the treacherous meandering in the formative years of open heart surgery—the risks, the dilemmas, the uncertainties, the disappointments—and the great satisfactions of making it work to deliver a life-sustaining service. Although Dr Frist provides the reader with some sense of the personal risk involved in his endeavor, he understates the potentially disastrous consequences to his career if his key decisions turn out to be wrong and his early results are less than expected. Perhaps this omission was deliberate or perhaps it derived from the confidence of his excellent preparation. He did, however, convey a strong sense of the collegiality in our profession that freely shares experience and advice when it comes to coping with a new problem or deciding about trying something that has never been done before.

Doctor Frist has achieved the rare and difficult objective of a book that is just as readable (and valuable) to the aspiring young cardiac surgeon as it is to the layman (and the other members of his profession who are laymen to transplantation).

Evaluating and recommending such a book from each of those viewpoints is difficult. Obviously it is not intended to be a professional text, yet I would commend it to my cardiac surgical colleagues for its insight and perspective. Nor does it pretend to be a fictional narrative as it names names and relates true experiences, yet it reads with suspense and compelling interest. Although it is not great literature or exciting drama, it is nonetheless both interesting and enjoyable. I recommend it to the full spectrum of readers.

San Francisco, California

Oxygen Free Radical Scavengers Decrease Reperfusion Injury in Lung Transplantation

Frank C. Detterbeck, MD, Blair A. Keagy, MD, Douglas E. Paull, MD, and Benson R. Wilcox, MD

Division of Cardiothoracic Surgery, University of North Carolina School of Medicine, Chapel Hill, North Carolina

An in vivo canine model was used to assess the ability of an oxygen free radical scavenger to decrease reperfusion injury in lung transplantation. In 12 dogs, the left lungs were transplanted after they had been preserved for 24 hours at 4°C after pulmonary artery flushing with modified Eurocollins solution. In 6 dogs, dimethylthiourea, a potent oxygen free radical scavenger, was added to the flush solution and was also given to the recipients just before reperfusion. In all animals, the contralateral pulmonary artery and bronchus were ligated and lung function was assessed for 12 hours or until death. Three dogs died prematurely in the control group, whereas only 1 dog died prematurely in the dimethylthiourea group. This resulted in a statistically significant difference in the average length of survival ($p < 0.05$). Pulmonary artery and right atrial pressures were significantly lower in the dimethylthiourea group during the first 6 hours ($p < 0.05$). Treatment with dimethylthiourea resulted in a significantly higher arterial oxygen tension at 4 hours, and intrapulmonary shunt tended to be lower. Thus, it would appear that dimethylthiourea has a protective effect on lungs preserved for 24 hours before transplantation in dogs.

(Ann Thorac Surg 1990;50:204–10)

Although lung transplantation is performed successfully at a number of centers around the world, the inability to preserve lungs safely for more than 4 to 6 hours represents a major impediment to more widespread applicability. Prolonged preservation results in a reimplantation response characterized by increased pulmonary capillary permeability, pulmonary edema, and respiratory failure [1]. This response appears to be due to cellular injury occurring not only during ischemic preservation but also during reperfusion after transplantation [2, 3].

Evidence is accumulating that reperfusion injury in many organ systems is mediated by oxygen free radicals. Ischemia sets the stage by alteration of metabolic pathways so that a large burst of toxic oxygen free radical formation occurs once oxygen is restored to the tissue. Thus, organ transplantation is a classic setting for oxygen free radical injury, and evidence is emerging that this injury plays a role in heart and kidney transplantation [4, 5]. In vitro experiments with isolated, perfused lungs have shown improved function and less edema formation with the addition of a variety of oxygen free radical scavengers during reperfusion [2, 3, 6–8]. Some in vivo data on the effect of oxygen free radical scavengers on lung function have recently appeared with similar results [9–11].

We have developed a canine model of single-lung transplantation after 24 hours of hypothermic storage. This model uses an initial pulmonary artery flush at the time of harvest, consistent with the method of lung preservation in most common clinical use in this country. One hour after transplantation the contralateral pulmonary artery is ligated, forcing the dog to survive solely on the 24-hour-preserved, transplanted lung while measurements are taken for the next 12 hours. Using this model, we set out to study the effect of dimethylthiourea (DMTU), a potent oxygen free radical scavenger, on in vivo lung function after preservation and reperfusion. Dimethylthiourea was chosen because of its long half-life, minimal toxicity in an in vivo setting, and potency as an oxygen free radical scavenger [12].

Material and Methods

Harvest

Twelve heartworm-negative mongrel dogs weighing 20 to 25 kg were anesthetized intravenously with 30 mg/kg of pentobarbital, intubated, and ventilated with room air. Through a left thoracotomy, both pulmonary arteries, main bronchi, and the left pulmonary veins were isolated. After intravenous administration of 5,000 U of heparin, cannulas were introduced into the left atrium and main pulmonary artery. Earlier experiments in our laboratory (unpublished) had shown that this did not affect pulmonary blood flow. The right pulmonary artery was ligated, and 1 mg of prostaglandin E_1 in 50 mL of normal saline solution was infused into the left pulmonary artery over 3 to 4 minutes. The infusion rate was adjusted as necessary to ensure that systemic hypotension did not occur. Thereafter, blood inflow to the main pulmonary artery was occluded, the left atrial cannula was opened to gravity drainage, and pulmonary artery flushing was begun.

Presented at the Thirty-sixth Annual Meeting of the Southern Thoracic Surgical Association, Scottsdale, AZ, Nov 9–11, 1989.

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0003-4975/90/$3.50

Flushing

A flush solution was mixed consisting of 1 L of Eurocollins solution at 4°C to which 4 mmol/L (8 mEq) of magnesium sulfate, 5,000 U of heparin, and 1 g of cephazolin were added. The left lung was perfused with 800 mL of this solution through a roller pump over an average of 4 minutes, during which the pulmonary artery pressure was kept less than 20 mm Hg and the lung was ventilated with room air. The left pulmonary artery and veins were clamped, and the left lung was excised with a cuff of left atrium and weighed. The lung was inflated with 100% N_2 at a pressure of 25 to 30 cm H_2O [8]. The bronchus was then clamped, and the lung was submerged in Eurocollins solution and stored at 4°C for 24 hours. The time between the onset of flushing and submersion of the lung, which averaged 12 minutes, was called the harvest time.

Recipient Preparation

Twelve recipient dogs, matched to within 2 kg of each respective donor, were anesthetized intravenously with 30 mg/kg of pentobarbital and intubated. The recipients were ventilated with 60% O_2 and a tidal volume of 400 mL, which was decreased to 200 mL when the right main bronchus was occluded. A Swan-Ganz catheter introduced into the right femoral vein was positioned in the main pulmonary artery, and aortic pressure was monitored with a catheter introduced through the femoral artery. A Millar pressure transducer was introduced into the left atrium, and an electromagnetic flow probe was placed around the left pulmonary artery. The right pulmonary artery and main bronchus were occluded with tourniquets for 5 minutes, baseline measurements were taken, and the tourniquets were released. The recipient was then given 2,000 U of heparin intravenously, and a left pneumonectomy was performed.

Transplantation

The 24-hour-preserved lung was allowed to deflate and then was weighed and wrapped with sponges soaked in iced saline solution. During transplantation, iced saline solution was continually dripped onto the lung. A left atrial anastomosis was performed with 5-0 Prolene suture (Ethicon, Somerville, NJ), air was evacuated, and all venous clamps were removed. The beveled pulmonary artery ends were then anastomosed with running 6-0 Prolene sutures, air was evacuated, and the vessel was unclamped. Finally, the bronchial ends were approximated with running 4-0 Prolene. The time between removal of the lung from the cold solution and restoration of blood flow to the lung was defined as transplantation time. The harvest time plus the transplantation time was defined as warm ischemic time.

Experimental Groups

The control group consisted of 6 dogs that had lung transplantations performed exactly as described. The DMTU group consisted of another 6 dogs that underwent lung transplantation, also performed exactly as described above except that DMTU was added to the flush solution at the time of lung harvest in a concentration of 50 mmol/L and an intravenous infusion of 1 g/kg of DMTU in 50 mL of normal saline solution was given to the recipient over 1 hour, timed so the infusion was complete by the time the pulmonary artery was unclamped after transplantation. Control and DMTU experiments were done in an alternating fashion to avoid any bias owing to experience.

Measurements

After left lung transplantation, a 1-hour stabilization period for both lungs was allowed. The right pulmonary artery and right main bronchus were then ligated, forcing the animal to survive solely on the preserved, transplanted lung. After 5 minutes, aortic and pulmonary arterial blood gas samples were drawn and pressures were recorded in the right and left atria, the pulmonary artery, aorta, and distal trachea. Cardiac output was obtained by an electromagnetic flow probe on the left pulmonary artery. An estimation of extravascular lung water was obtained by the thermal-thermal method using an Edwards Lung Water Computer (American Edwards Laboratories, Irvine, CA) by averaging three determinations [13]. All measurements were repeated hourly for 8 hours. Two further sets of measurements were obtained at 10 and 12 hours after transplantation, at which time the animals were killed. The animals' chests were reopened, and the left lung was removed and weighed. After the lungs were dried in an oven to a stable dry weight, wet/dry weight ratios were calculated.

Maintenance

A transient drop in cardiac output was observed when the transplanted lung was unclamped, and this was counteracted by administration of calcium chloride. One gram of cefazolin was also given during the 1-hour stabilization period after transplantation. When the right pulmonary artery and main bronchus were ligated, the tidal volume was decreased to 200 mL, and the chest was loosely closed. The ventilatory rate was adjusted to maintain partial pressure of carbon dioxide between 35 and 45 mm Hg, but the inspired oxygen concentration was maintained at 60%. Endotracheal suctioning was performed at least every 30 minutes, and more often if necessary. Sodium bicarbonate was given to maintain arterial pH at 7.30 to 7.40. Ringer's lactate was given to maintain the left atrial pressure at 4 to 7 mm Hg, and no inotropic or vasodilator agents were used. No interventions were made within the 15 minutes before a measurement. Body temperature was maintained at 36° to 37°C by the use of heating pads and warmed intravenous fluids. Sedation was maintained using a continuous infusion of chloralose at 12.5 mg/kg/h.

Statistics

For statistical analysis, data obtained during the study period were grouped into 2-hour time blocks. The results depicted at each time point are therefore the average of two measurements taken from each animal during that time block. All results were analyzed using a two-tailed *t*-test. A *p* value less than 0.05 was considered statistically

Table 1. Characteristics of Experimental Groups

Characteristic	Control	DMTU	*p* Value
Animal weight (kg)	24.0	21.0	NS
Preservation (h)	24.6	24.9	NS
Warm ischemia (min)	72.2	74.5	NS
Average survival (h)	8.5	11.8	0.05
Wet/dry lung weight	7.97	7.70	NS

DMTU = dimethylthiourea; NS = not significant.

significant. Variability is presented as the standard error of the mean and is depicted by error bars on the graphs, with the exception of pulmonary vascular resistance, in which error bars depict one half the standard error of the mean.

Humane Treatment

This study was approved by the Institutional Animal Care and Use Committee of the University of North Carolina. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985).

Results

Both groups were comparable with respect to animal weights, duration of preservation, and warm ischemic time, as shown in Table 1. In the control group, 3 recipients died at 2, 4, and 8 hours after completion of the transplantation, whereas in the DMTU group only 1 animal died at the 11-hour time point. The longer average length of survival in the DMTU group was statistically significant.

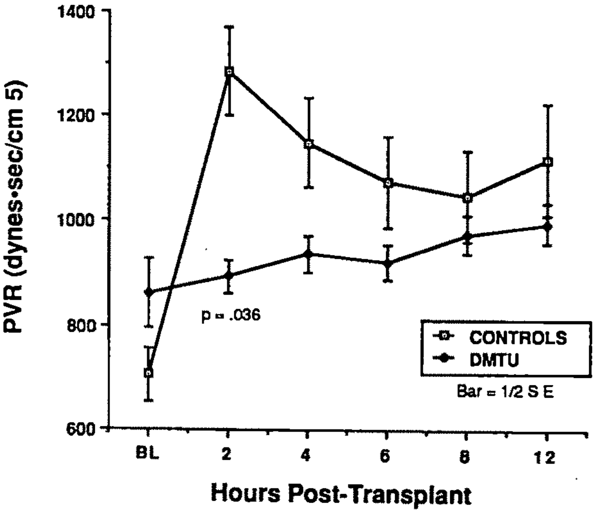

Fig 2. Pulmonary vascular resistance (PVR) versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea; SE = standard error.)

Pulmonary artery pressures on reperfusion were consistently lower in the DMTU-treated group, as shown in Fig 1. There was marked statistical significance for the differences during the first 6 hours. Pulmonary vascular resistance was also lower in the DMTU group (Fig 2) as might well be expected as there were no differences in the cardiac output between groups. Owing to larger variability, however, this was statistically significant only during the first 2 hours. There was no difference in aortic pressure, heart rate, or airway pressure. Right atrial pressure was significantly higher in the control animals (Fig 3). Left atrial pressures were not significantly different between groups.

Arterial oxygen tension was significantly higher in treated animals at 4 hours (Fig 4). Calculated intrapulmonary shunt tended to be lower in treated animals, but this was not statistically significant. Furthermore, there was a continual rise in intrapulmonary shunt throughout the course of the experiment in both groups (Fig 5). Extravas-

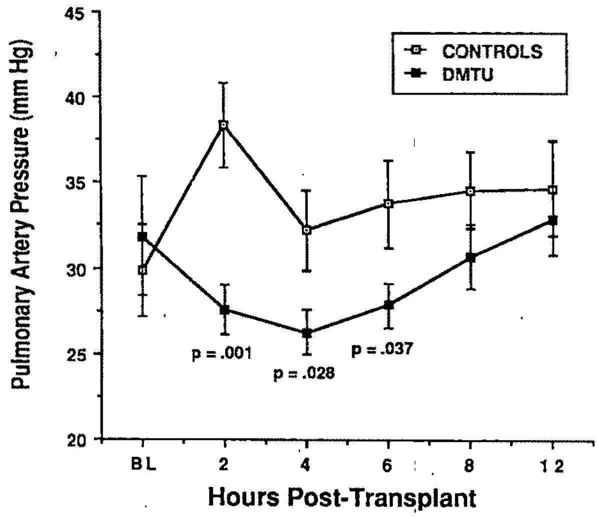

Fig 1. Pulmonary artery pressure versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

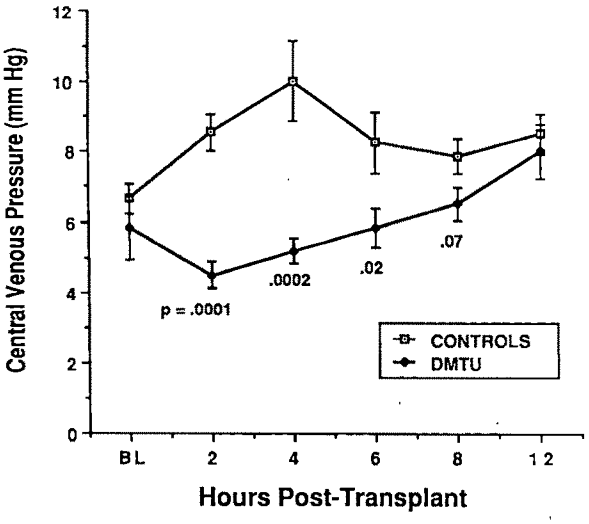

Fig 3. Central venous pressure versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

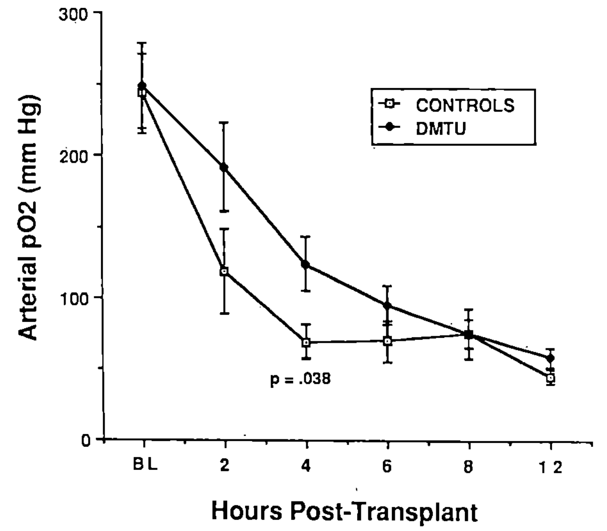

Fig 4. Arterial oxygen tension (pO2) versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

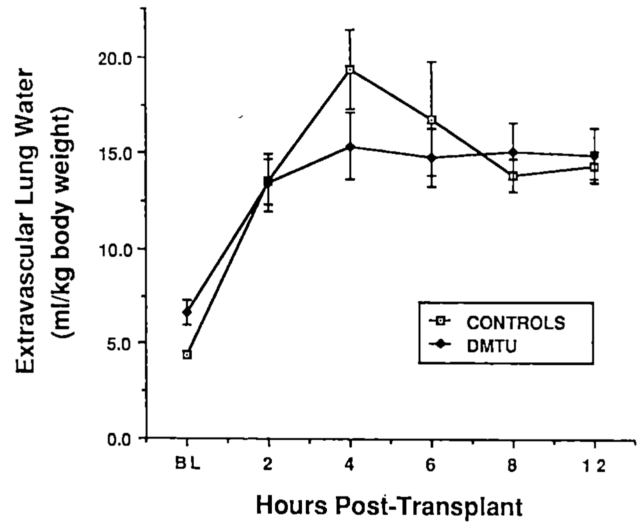

Fig 6. Extravascular lung water versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

cular lung water measurements showed an early steep rise followed by a plateau (Fig 6). There was no statistically significant difference between groups, although the controls tended to have higher values at 4 hours. There were also no statistically significant differences in the wet/dry lung weight ratios after drying of the lung (Table 1).

Comment

Ischemia followed by reperfusion is associated with the production of oxygen free radicals at the time of reperfusion [2]. These are very reactive compounds that damage the molecular structure of proteins and cell membranes by triggering a chain reaction of lipid peroxidation. They are produced by at least two sources: neutrophils that have become activated during ischemia, and the degradation of adenosine after ischemia [3, 14]. Xanthine dehydrogenase, the normal enzyme responsible for this degradation, is converted to xanthine oxidase during ischemia, which then produces oxygen free radicals when accumulated adenosine is metabolized during reperfusion. Pulmonary endothelial cells seem to be particularly affected [15], and the cell membrane damage leads to cell edema and capillary obstruction ("no reflow phenomenon").

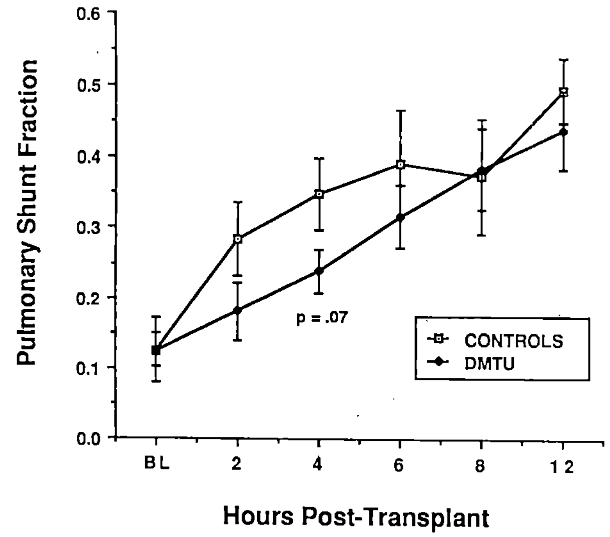

Fig 5. Pulmonary shunt fraction versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

Several in vitro studies with isolated perfused lungs have suggested that this reperfusion injury plays an important role in poor lung function after preservation. Rabbit lungs preserved for 24 hours and then reperfused with leukocyte-poor blood showed significantly less edema formation, better preservation of histological structure, and a lower vascular resistance compared with those reperfused with normal blood [14]. Lower pulmonary artery pressures, less edema, and less albumin leakage into the alveoli after 2 hours of 37°C ischemia have also been demonstrated after pretreatment with lodoxamide, a xanthine oxidase inhibitor [3]. We have previously demonstrated less edema and lower pulmonary artery pressures with the addition of oxygen free radical scavengers such as DMTU or superoxide dismutase and catalase in isolated lung models [2, 6, 16]. This has been confirmed by other investigators as well [7, 17].

The current study also demonstrates lower pulmonary artery pressures throughout the course of the study with the addition of DMTU. In previous unpublished experiments, we have found the same dose of DMTU to have no hemodynamic effect in anesthetized dogs. Wong and colleagues [18] have reported a transient slight increase in pulmonary artery pressures in pigs after infusion of 0.5 g/kg of DMTU, whereas others [4, 19] have reported no effect of intravenous DMTU on cardiac output, aortic pressure, or pulmonary artery pressures. Thus, we believe that the lower pulmonary artery pressures demonstrated in this study are not due to a direct hemodynamic effect of the DMTU itself.

Both a variety of oxygen free radical scavengers and a number of xanthine oxidase inhibitors have been shown to decrease pulmonary artery pressures on in vitro reperfusion after lung preservation [3, 6, 7, 16]. In vitro experiments have also shown that this effect correlates well with decreased lipid peroxidation, decreased endothelial cell permeability, and a decrease in markers of endothelial cell injury [2, 3, 6, 15, 17]. This suggests that the lower pulmonary pressures observed in the current study are due to a decrease in oxygen free radical–induced injury, which might be due to decreased endothelial cell swelling or less thrombotic plugging of severely damaged capillary beds. Alternatively, this might be due to less vasoconstriction, possibly mediated by decreased thromboxane levels in the presence of oxygen free radical scavengers. Oxygen free radicals have been shown to increase thromboxane levels [20, 21], and some authors have suggested this is due to metabolism of arachidonic acid released from oxygen free radical–damaged cell membranes [21].

Intravenous fluids were given to maintain left atrial pressure and cardiac output, and no difference between the groups was observed in these variables. Also, there was no statistically significant difference in the amount of fluid given. Thus, the higher right atrial pressures observed in the control dogs do not represent a difference in fluid management, but rather demonstrate a degree of right heart dysfunction owing to the elevated pulmonary vascular resistance. Dimethylthiourea was effective at keeping right atrial and pulmonary artery pressures closer to baseline single-lung perfusion levels.

Arterial oxygen tension tended to be higher in the DMTU group, but differences were statistically significant only at 4 hours. The same pattern was observed for calculated intrapulmonary shunt. Despite lower shunt levels at most of the time points with DMTU, there was a constant rise in shunt fraction throughout the experiment. Decreased interstitial and alveolar edema as a result of oxygen free radical scavengers could explain better oxygenation. Part of the reason for a lack of statistical significance in the later measurements is undoubtedly the smaller number of measurements available owing to the death of several of the controls. This also skews the data somewhat, in that the controls that were still alive at later time points were a select group with better oxygenation than the other control animals.

It is not clear, however, why lung function should deteriorate with time. It is possible that DMTU was consumed during the first few hours and was therefore no longer able to protect the lung against reperfusion injury. However, there is evidence that reperfusion injury occurs only in the first hour after reperfusion [14]. The dose of DMTU used has also been shown to be enough to scavenge the oxygen free radicals produced by maximally stimulated neutrophils over a 45-minute period [16, 17, 22]. The plasma half-life of DMTU in the absence of increased oxygen free radical production has been shown to be 24 to 36 hours in several mammalian species [4, 17, 22]. A dose of 500 mg/kg of DMTU every 12 hours has been effective at preventing much of the pulmonary injury seen in rats subjected to 100% O_2 for 2 days [22], a situation thought to be associated with increased oxygen free radical production. Therefore, although no data on DMTU consumption in this particular setting of lung ischemia and reperfusion are available, we believe it is unlikely that the DMTU was consumed during the first few hours.

We believe it is much more likely that the progressive lung deterioration was due to a severe injury from the prolonged ischemia alone. Although DMTU was able to attenuate some of the reperfusion injury, we think that these lungs had suffered serious preservation injury, which caused many endothelial and parenchymal cells to undergo cell death despite the addition of DMTU. The oxygen free radical scavenger may have merely postponed the cell death by altering the immediate cause rather than affecting the final outcome in lungs subjected to 24 hours of ischemia.

This would also explain the lack of difference in extravascular lung water. Although wet lung weights at the termination of the study were higher in the control group, the ratio of wet to dry weight, which is a better measurement of lung water, failed to show any difference. The in vivo extravascular lung water determinations suggested increased edema in the control group at 4 hours, but a greater difference may have been masked by the edema caused by the ischemic injury alone. Furthermore, the capillaries in the areas of lung most severely injured may have swollen to the point of obstruction, thus rendering these areas incapable of any further fluid retention.

Some authors have indicated that lung weight gain after ischemia occurs early and is a sensitive indicator of the degree of ischemic/reperfusion injury [23, 24]. We agree that most of the edema has occurred by 4 hours, but we found that this does not correlate well with lung function or ultimate survival, as a continued deterioration in these variables was observed. Our results also suggest that animals must be followed up for a considerable period of time (at least 6 hours) before the effect of long-term lung preservation can be assessed realistically. By our assessment, oxygenation correlated closely with survival and is the best measure of the quality of lung function. These experiments also serve to underscore once again the difficulty of extrapolating from in vitro data to in vivo results.

In summary, we have shown decreased pulmonary artery pressures and better oxygenation after 24-hour lung preservation by the addition of DMTU in an in vivo lung transplantation model. However, a continued gradual deterioration of lung function was also observed during the 12-hour posttransplantation measurement period. No major differences in extravascular lung water were observed. We believe this is evidence that oxygen free radical scavengers do reduce lung reperfusion injury in vivo, but that severe lung injury owing to the 24-hour preservation alone still remains. Experiments are underway to assess the effect of varying the duration of preservation in the presence of oxygen free radical scavengers.

We gratefully acknowledge the assistance of Eric Kron, whose dedication, thought, and vigilance were crucial in carrying out the experiments, and of Betsy Mann, who transcribed and edited the manuscript.

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DISCUSSION

DR J. KENT TRINKLE (San Antonio, TX): I am very impressed with the fact that you have been able to preserve lungs for 24 hours; that is extraordinary. We have been using essentially your control, donor prostaglandin E_1 infusion, followed by 1,500 mL of modified Eurocollins topical slush. We have used this in 18 patients, 6 heart-lung and 12 lung transplantations, but our procedures have never gone longer than just a little over 4 hours. The last transplantation we performed just two nights ago was on a single lung of a man with chronic obstructive pulmonary disease. His initial partial pressure of oxygen was 516 mm Hg. I think this is about as good as you are going to get in the acute clinical setting. We are also looking at the free radical scavenger glutathione in the laboratory, and we have just started with the UW solution, which, of course, has the scavengers and a hodgepodge of other things, too.

I think the main value of this may be in the high responders in whom you need time to do a lymphocyte cross-match. With our current technology, there is not a whole lot of reasons to perform an operation beyond 5 or 6 hours unless you like to operate at 8 AM instead of 2 AM or the like, as we all do in this business. Anyway, it is obvious that this is going to be the wave of the future. I do not know whether we will ever get to do lung transplantation as a semielective case like in kidney transplantation; but in the acute stage, I do not think there is a whole lot of advantage. In prolonged preservation, there is no question but that this is the way to go.

DR JAMES STEWART (Nashville, TN): I was wondering, did you measure any lipid peroxidation products or any other index of free-radical injury in the lung tissues?

DR DETTERBECK: No, we did not measure that in this paper. We have done that previously in vitro in experiments, and we did find an increase in thiobarbituric acid consistent with other measures, increased lung edema, and decreased oxygenation of the lung. We did not do that in this study.

DR STEWART: We have been interested in this problem as well, and I am trying to dissect out some of the causes of the reimplantation response. It is interesting to note that if you devascularize and denervate the lungs of sheep but leave them in place and put balloon occluders on the bronchus and on the pulmonary artery as well as the pulmonary vein, you can occlude them and by microspheres show no flow into that lung; and if you reperfuse them 24 hours later, they show no response at all. I do not know why.

DR WILLIAM A. COOK (North Andover, MD): Do you have any idea what the effect of DMTU may be on the surface of the circulating cells?

DR DETTERBECK: No, I am not aware of any studies that anyone has done looking at that.

DR COOK: The reason I ask is I was struck by the high pulmonary artery pressures that developed immediately after you had started your reliance on the transplanted lung. This looked very similar to the pressures in a shock-lung preparation in which the problem is direct mechanical blockade of the pulmonary capillaries by clumps of cells.

DR DETTERBECK: Well, I am not aware of any data to answer this question. People have looked at the effect of DMTU, and we did look as well in our laboratory, just giving DMTU to normal animals, but could find no effects on pulmonary blood pressure, cardiac output, or aortic blood pressure. There were no hemodynamic effects whatsoever.

Leukocyte Depletion Results in Excellent Heart-Lung Function After 12 Hours of Storage

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Bruce A. Reitz, MD, and William A. Baumgartner, MD

The Johns Hopkins Hospital, Baltimore, Maryland

Extended preservation of the heart-lung bloc for 12 hours in a bovine model of heart-lung transplantation was achieved using donor core cooling, static hypothermic storage, and reperfusion on cardiopulmonary bypass with leukocyte-depleted (LD) blood. Orthotopic heart-lung transplantation was performed with (n = 4, LD group) or without (n = 4, control group) LD blood during cardiopulmonary bypass. Postoperative measurements of cardiopulmonary function were made at 2, 4, and 6 hours after reperfusion. Only 2 animals (50%) of the control group survived more than 2 hours, whereas all animals in the LD group survived the study period. Arterial oxygen tension on 100% oxygen was 535.63 ± 64.96 mm Hg and 146.45 ± 90.9 mm Hg in the LD and control groups, respectively, at 2 hours ($p < 0.5$) and 524.3 ± 73.32 and 147.9 ± 255.67 mm Hg at 6 hours. Pulmonary artery systolic pressure-to-systemic pressure ratio was 0.49 ± 0.08 and 0.62 ± 0.35 at 2 and 6 hours in the LD group. Extravascular lung water was 17.81 ± 0.02 mL/kg (control group) and 11.28 ± 9.15 mL/kg (LD group) at 2 hours. At reperfusion, the mean neutrophil count was 27 ± 27 and 764 ± 635 × 10^9/L in the LD and control groups, respectively. This novel approach of leukocyte depletion during reperfusion after heart-lung preservation resulted in excellent cardiac and pulmonary protection.

(Ann Thorac Surg 1990;50:211–4)

Clinical heart-lung and lung transplantation has progressed rapidly since the first successful long-term outcome was reported by Reitz and co-workers in 1981 [1]. The limitation in the number of patients treated remains one of donor availability, which has been in part due to the lack of techniques of long-term organ preservation. Most currently used methods of clinical preservation have extended preservation times to 4 to 6 hours.

Experimental studies have increasingly demonstrated the role of oxygen free radicals in causing serious lung injury at the time of reperfusion. In addition, the role of neutrophils in lung injury at the time of reperfusion after a period of ischemia has been demonstrated in vitro [2]. Furthermore, a recent study evaluating the effect of leukocyte depletion in a canine model of cardiopulmonary bypass showed the effectiveness of the depletion technique as well as the improved physiological outcome, particularly regarding lung function in a canine model [3]. Using this technique of leukocyte depletion on cardiopulmonary bypass, we have evaluated the effectiveness of such depletion on preservation of heart and lung function after 12 hours of static hypothermic storage of the heart-lung bloc in a bovine model of orthotopic heart–lung transplantation.

Material and Methods

Eight dairy calves (mean weight, 39.7 kg) underwent orthotopic heart-lung transplantation from size-matched donor animals using established techniques [4]. The animals were divided into two groups. In both groups, core cooling on cardiopulmonary bypass was the technique of cardiopulmonary preservation. After such cooling and cardioplegic cardiac arrest, in the control group (n = 4), the organ bloc was stored in cold donor blood at 4°C. In the leukocyte-depleted (LD) group (n = 4), leukocyte filters (Pall RC 100, Pall Biomedical Products Corporation, Glen Cove, NY) were incorporated in the extracorporeal circuit between the roller pump and the arterial filter during organ procurement as well as at the time of orthotopic allotransplantation. Organs were similarly stored for 12 hours.

Donor animals were pretreated intramuscularly with ketamine hydrochloride (0.2 mg/kg), and anesthesia was induced intravenously with sodium pentobarbital (5 to 7 mg/kg). After endotracheal intubation, animals were placed on a volume-cycled ventilator with a tidal volume of 15 mL/kg at 15 to 20 breaths/min. The fraction of inspired oxygen was maintained at 100%. All animals were paralyzed with pancuronium bromide (0.05 to 0.1 mg/kg, intravenously). After median sternotomy, a 5F thermistor-tipped catheter (lung water catheter, American Edwards Laboratory) was placed into the internal mammary artery for continuous arterial pressure monitoring and for measurement of extravascular lung water. A 7F balloon-tipped thermodilution catheter (Swan-Ganz cath-

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eter, American Edwards Laboratory) was placed through the superior vena cava into the distal pulmonary artery.

Baseline functional data were obtained from all donor animals. These included systemic arterial, pulmonary arterial, pulmonary capillary wedge, and central venous pressures. Arterial blood gases were analyzed using an ABL-30 acid–base analyzer (Radiometer). Measurements of thermodilution cardiac output and extravascular lung water were obtained through the lung water catheter. The latter determinations were on the basis of a double-indicator dilution method using a cold sterile dye solution (5 mg indocyanine green dye in 10 mL D5W at 5°C) injected into the superior vena cava. Static lung compliance was calculated using tidal volumes and peak airway pressures measured by a catheter placed in the endotracheal tube and connected to a pressure transducer.

After collection of baseline data, donor animals were systemically heparinized (3 mg/kg) and placed on cardiopulmonary bypass at a rate of 2.5 to 3.0 L/min. The animals were cooled to a core (pharyngeal) temperature of 12° to 15°C, and the left atrial appendage was incised to prevent left ventricular distention. On reaching a temperature of less than 15°C, the heart was arrested with cold cardioplegic solution (15 mL/kg) instilled into the aortic root. The aorta, vena cava, and trachea were then divided, and the heart-lung bloc was excised with the lungs inflated to 70% capacity. The bloc was immersed in cold blood obtained from the oxygenator and stored in sterile conditions at 4°C.

Recipient animals were similarly anesthetized. Cardiopulmonary bypass was instituted after median sternotomy, and the temperature was allowed to drift. The lungs and heart were excised as described previously, and the stored heart-lung bloc was implanted. The animals were fully rewarmed and were weaned off cardiopulmonary bypass. At the completion of the study, the animals were killed by an overdose of pentobarbital.

All animals received humane care in compliance with "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Statistical analysis was performed using Student's t test, and all results are presented as means plus or minus one standard error. A p value of less than 0.05 was considered significant.

Results

Only 2 animals (50%) in the control group survived more than 2 hours. Death was preceded by substantially raised pulmonary artery pressure, severe pulmonary edema, and right ventricular failure. In the LD group, 100% survived the 6-hour study period.

The pulmonary artery to systemic artery pressure ratio was 0.49 ± 0.08 and 0.62 ± 0.35 at 2 and 6 hours, respectively. Arterial oxygen tension on 100% oxygen was 535.63 ± 64.96 mm Hg and 146.45 ± 90.9 mm Hg in the LD and control groups, respectively, at 2 hours and 485.15 ± 82.54 mm Hg and 147.9 ± 255.67 mm Hg at 6 hours. This difference was significant ($p < 0.05$) (Fig 1). Extravascular lung water measurements were similarly increased in the control group but decreased at 6 hours with worsening pulmonary edema in the 2 animals that survived (Fig 2). Lung compliance, however, was similar in both groups. Cardiac function was well preserved in all survivors (Fig 3). At reperfusion, the mean neutrophil count was 27 ± 27 and 764 ± 635 × 10^9/L in the LD and control groups, respectively. Baseline measurements were similar in both groups.

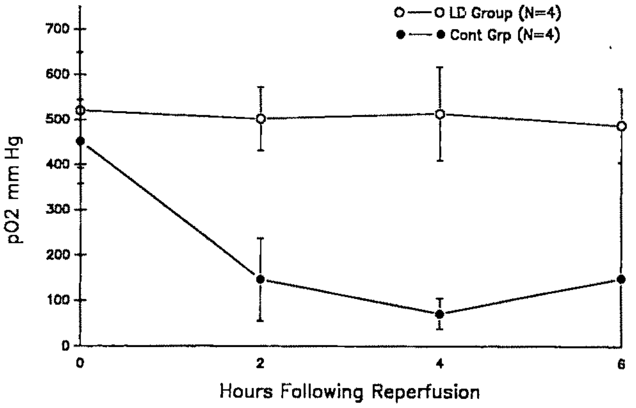

Fig 1. Comparison of oxygenation after reperfusion. (Cont = *control;* LD = *leukocyte-depleted;* pO_2 = *oxygen tension.)*

Postmortem histological examination of the lungs showed focal alveolar injury accompanied by intravascular leukocyte aggregation and perivascular hemorrhage to a much greater extent in the control group when compared with the LD group (Fig 4).

Comment

The protective effect of antioxidant scavengers in preserving lung function after reperfusion was demonstrated in an in vitro model of an isolated rabbit lung by Stuart and co-workers in 1985 [5]. They showed the effect of catalase and superoxide dismutase in extending the cold ischemic

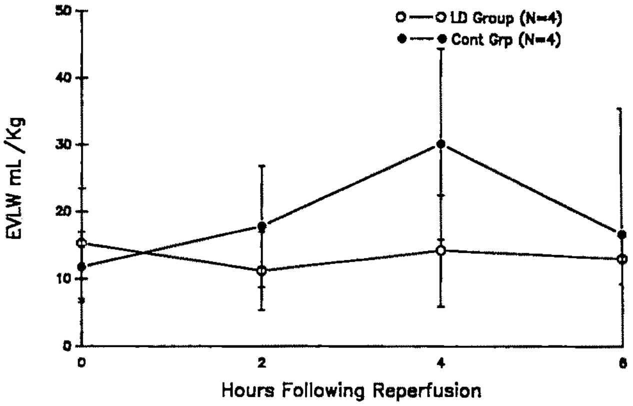

Fig 2. Change in extravascular lung water (EVLW) *after reperfusion.* (Cont = *control;* LD = *leukocyte-depleted.)*

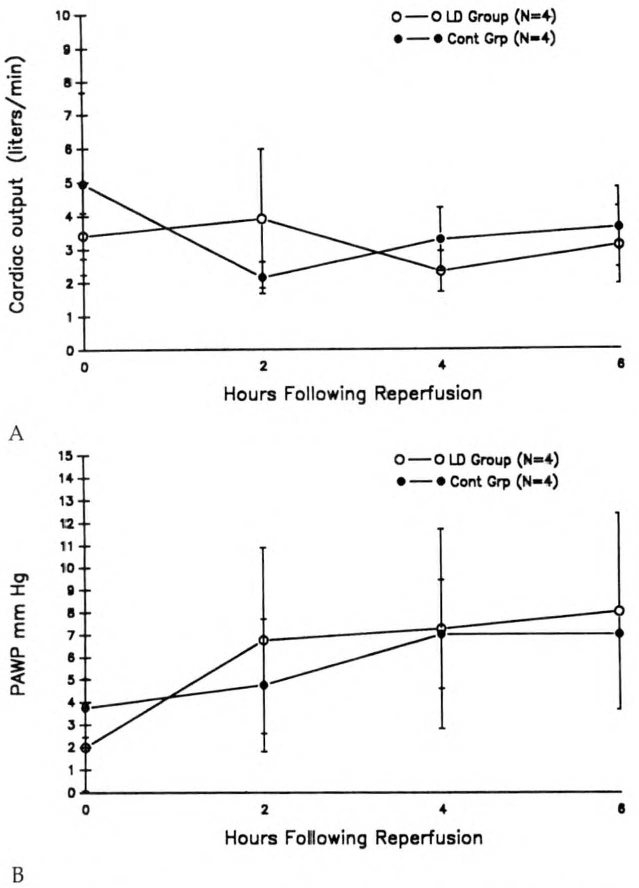

Fig 3. Cardiac function after 12 hours of static preservation: (A) cardiac output, and (B) pulmonary artery wedge pressure (PAWP). (Cont = *control;* LD = *leukocyte depleted.)*

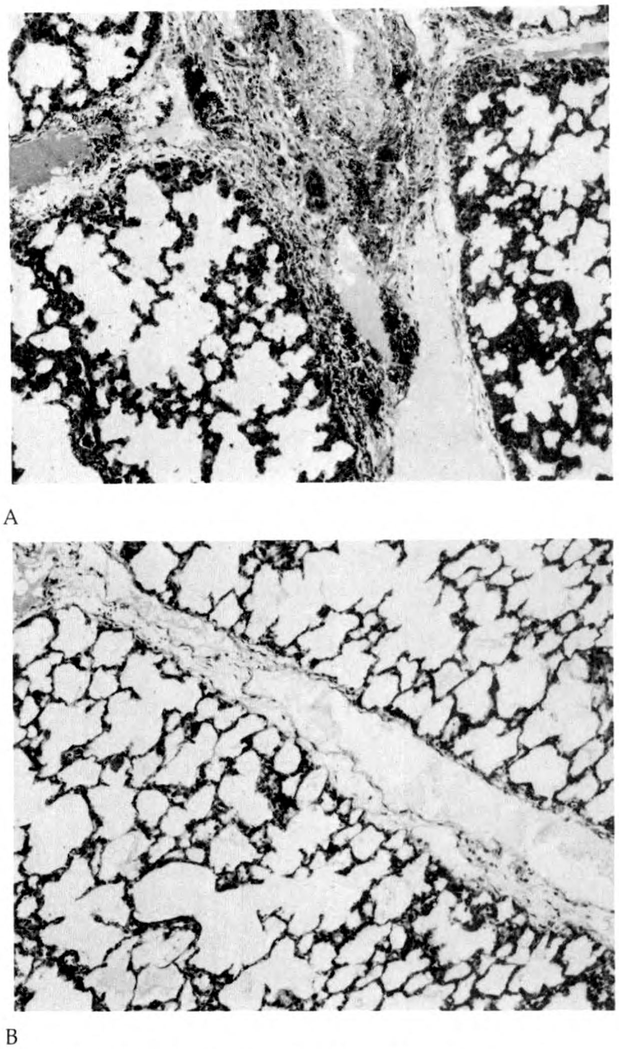

Fig 4. Histological appearance of the lung (A) in the control group and (B) in the leukocyte-depleted group.

period to 12 hours. The beneficial effects of such scavengers was shown to extend the preservation period to 8 hours in an in vivo model by Bando and colleagues in 1989 [6].

It may be postulated that the production of oxygen free radicals by the xanthine oxidase pathway results in the production of chemotactic factors after metabolism of arachidonic acid [7, 8]. This process itself leads to the sequestration and activation of neutrophils with further production of oxygen radicals and the formation of potent cytotoxic halide radicals via the myeloperoxidase pathway (Fig 5) [9]. In a previous study in our laboratory [3], we demonstrated the effect of leukocyte depletion on plasma conjugated dienes. The increased formation of plasma conjugated dienes in the control group suggests greater activity of oxygen free radicals leading to lipid peroxidation.

In the setting of reperfusion of the lungs with the use of cardiopulmonary bypass, the resulting activation of complement with the production of activated C5a moiety results in the sequestration and activation of neutrophils [4, 10, 11]. Several studies have shown that neutrophil sequestration in the lung leads to the release of a wide variety of vasoactive and cytotoxic agents culminating in the destruction of lung tissue. This effect produces the changes in alveolar capillary permeability and the loss of normal lung architecture on histology. Physiological alterations in pulmonary vascular resistance and efficacy of gas exchange are parallel features.

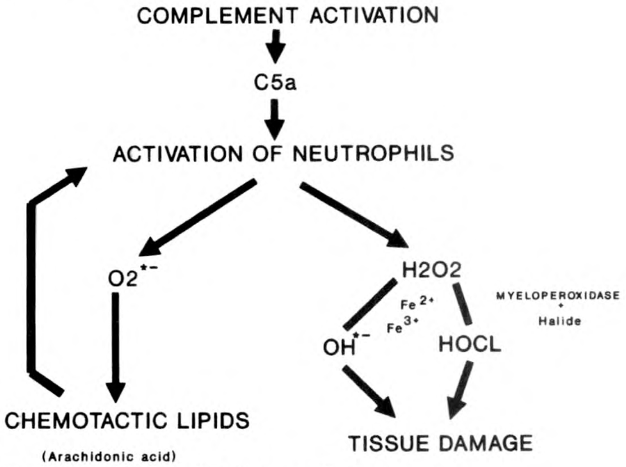

Fig 5. Role of neutrophils in free radical generation.

In addition, there is the known sensitivity of the alveolar endothelium to oxygen radical damage owing to certain morphological and biochemical characteristics. These include the large lipid membrane surface with a relatively reduced complement of intracellular organelles, which in turn may cause a further limitation of the antioxidant capabilities of alveolar endothelial cells, particularly as they are juxtaposed to the bloodstream and its contents [12, 13].

Further evidence for the role of neutrophils in such lung injury is demonstrated by the protective effects of neutrophil depletion. Indeed, reperfusion with LD blood protects lungs ischemic for 5 to 24 hours against reperfusion injury [14]—an effect not altered by readdition of autologous leukocytes 1 hour after initial reperfusion [2]. In vitro [2, 15] and in vivo studies using animal models [3] have shown that lung injury measured by morphological and physiological variables is markedly attenuated in the absence of circulating neutrophils.

This novel approach of neutrophil depletion on cardiopulmonary bypass with successful preservation of the heart-lung bloc for 12 hours further supports the role of oxygen free radicals and neutrophils in the injury caused to lungs at the time of reperfusion.

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DISCUSSION

DR SAFUH M. A. ATTAR (Baltimore, MD): This is a very nice study; however, I find one objection—these conclusions cannot be really based on a very small series. You have a series of 4, and I think it is too small to be significant; therefore, I think the study must be extended so that you can draw those conclusions.

DR PILLAI: I agree with that. The study is being extended.

DR ANDREW S. WECHSLER (Richmond, VA): You said that you stored the hearts in blood. I assume it was oxygenated blood that you stored them in and it was cold.

DR PILLAI: That is right.

DR WECHSLER: What was the oxygen concentration at the end of the storage period in the blood? Are you postulating a reoxygenation mechanism as playing a role in the injury that you may have prevented by the leukocyte depletion?

DR PILLAI: We did randomly test the oxygenation of the blood at the end of the preservation period, and it was more or less the same as at the beginning. In terms of oxygenation, I think it is a difficult problem that needs to be evaluated, but we know from clinical practice that in some ways empirically we have not reinflated lungs after a period of ischemia with more than about a 40% or 50% inspired oxygen fraction. This is based on worries about reperfusion injury due to oxygen free radicals. We ventilated all our animals and post-weaned them on 100% oxygen in both groups.

Sclerosing Mediastinitis: Improved Management With Histoplasmosis Titer and Ketoconazole

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Recognition that many patients with benign sclerosing mediastinitis have smoldering disease responsible for failure of surgical procedures or for development of collateral circulation in patients with superior vena caval obstruction has markedly improved management of these difficult patients. Histoplasmosis complement fixation titers have been used to detect unsuspected subacute disease and to follow the therapeutic adjunctive management with ketoconazole, an oral antifungal agent. Twenty-two patients with benign sclerosing mediastinitis demonstrated a variety of symptoms relating to the area of compression: superior vena cava, 13; esophagus, 3; pulmonary artery and pericardium, 3; and trachea, 3. Histoplasmosis was documented in 12 patients. Operation is used initially for diagnosis, to rule out carcinoma, and to treat the complications: superior vena caval reconstruction, 6; tracheal decompression, 2; right middle lobectomy, 1; esophageal decompression, 2; division of tracheoesophageal fistula, 1; and release of pericardial effusion and cardiac tamponade, 1. Postcardiotomy syndrome occurred in 1 patient and wound infection in another. No deaths resulted. In 6 cases of histoplasmosis, symptoms recurred in 100% of patients and were successfully managed with ketoconazole treatment, and then clinical progress was monitored with serial histoplasmosis complement fixation studies. One patient had four superior vena caval reconstructions at an outside hospital, each 1 year apart, with symptoms recurring each time. With ketoconazole therapy alone, she has been asymptomatic for more than 2 years. Vigorous search for a fungal cause may even obviate the necessity for surgical intervention. If an operation is necessary, preoperative and postoperative use of ketoconazole has assured success.

(Ann Thorac Surg 1990;50:215–21)

Sclerosing mediastinitis and *fibrosing mediastinitis* are equivalent terms that describe a process of acute and chronic inflammation resulting in progressive fibrosis within the mediastinum [1–5]. The process usually involves the superior mediastinum and is a relentless proliferation of fibrous tissue that produces encroachment, entrapment, and eventual compression of the mediastinal structures. It affects primarily and initially the low-pressure structures such as the superior vena cava (SVC) [6]; the azygos, innominate and pulmonary veins [7]; and the pulmonary arteries [8]. It also may involve the esophagus and trachea [9, 10] and can be caused by a variety of organisms [11–16].

In the past, an operation was used to establish the diagnosis, rule out carcinoma, and provide decompression of the entrapped organs [17–20]. More recently, recognition that a subacute phase of active disease may coexist or smolder in a process that appears to be a burned-out clinical entity may reduce the necessity of an operation in some patients. The importance of this finding has been the ability to treat this subacute inflammation with ketoconazole, effectively reducing compression and ameliorating symptoms. This unrecognized inflammation process may also be responsible for the frequent failure of surgical decompression or bypass in patients with superior vena caval obstruction (SVCO).

This paper reviews cases of 22 patients with sclerosing mediastinitis managed over a period of 25 years.

Material and Methods

Patients

Twenty-two patients were followed over 25 years with the diagnosis of benign sclerosing mediastinitis. There were 14 female and 8 male patients ranging in age from 14 to 64 years (mean age, 46 years). These patients were seen with a variety of symptoms at varying stages in their diagnosis and management. Some came for initial diagnosis and treatment whereas others were treated extensively elsewhere; some had multiple surgical procedures and were referred for further management.

Cause

All patients had been explored surgically to rule out any malignant process and to establish the diagnosis whenever possible. The diagnosis of histoplasmosis has been established by smear or culture of the biopsy specimens or by complement fixation studies showing an increasing titer over time in 12 of the 22 patients (6 of 6 of the last

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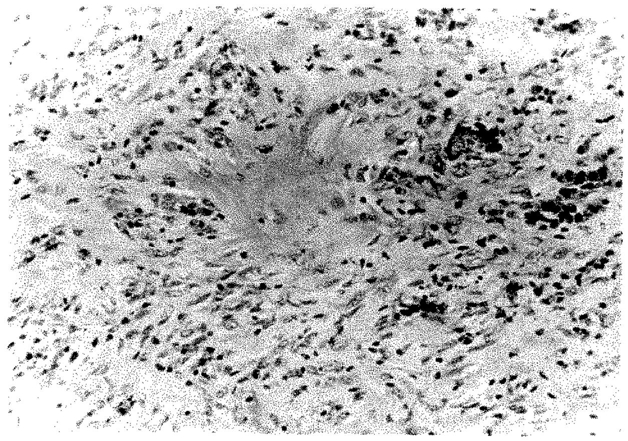


Fig 1. Photomicrograph showing bands of collagen with inflammatory infiltrate and areas of hyalinization.

group of patients evaluated clinically). Nine patients failed to show any cause and were designated idiopathic. However, these patients were managed in the early part of the study when the search for causal agents was not as extensive as it is today, particularly with respect to the use of complement fixation studies. Tuberculosis was documented in 1 patient early in the series as the cause of the disease.

Pathology

Intraoperatively, the observed gross pathology is that of a dense, scirrhous, homogenous, fibrous tissue encasing the mediastinal structures causing total obliteration of tissue planes. (The stony hard consistency of the fibrous tissue and its intimate involvement of the vital mediastinal structures made tissue extirpation a hazardous undertaking.) Microscopically, the resected tissues showed dense collagen bands with activated fibroblasts and inflammatory cellular infiltrate composed mainly of mature lymphocytes and plasma cells. The collagen bands are interspersed by an area of hyalinization (Fig 1). A striking feature was the presence of arteriolar obliteration caused by intimal hyperplasia and medial thickening. Vasculitis was not present as evidenced by the absence of necrosis and of inflammatory cell infiltrate of the vessel wall (Fig 2).

In 1 patient, multiple caseating granulomas were also present in the area adjacent to the fibrosis. Budding yeast forms were visualized in the areas of caseation consistent with *Histoplasma capsulatum* (Fig 3).

Diagnosis

Superior vena caval obstruction was observed in 13 of 22 patients. Compression symptoms in 13 patients included swelling and edema of the upper extremities, face, and the anterior chest wall as well as an increase in dilated superficial veins and flushing in these areas. Central nervous system symptoms occurred in 3 patients, headache in 1, nausea in 1, and dizziness with visual disturbance in 1. The esophagus was compressed producing dysphagia in 3 patients, and tracheal compression in 3 patients caused intermittent stridor, shortness of breath, dyspnea, and positional changes requiring the patients to sleep in an upright position. The pericardium was involved in 2 patients, in 1 by bleeding and tamponade and in another by postcardiotomy syndrome with evidence of pericarditis. The pulmonary artery was obstructed or compressed in 1 patient producing pulmonary hypertension and symptoms like mitral stenosis.

After going through a careful medical history review and physical examination, the patient underwent routine chest roentgenography and a computed tomographic scan of the neck, chest, and upper abdomen. These scans usually revealed widening of the mediastinum without any other evidence of mass lesions or other important causes. In the patients with SVCO, simultaneous bilateral brachial venograms were conducted showing the anatomy of the veins of the upper extremity and the innominate vein, and the area of obstruction and degree of compression of the SVC. The venograms also demon-

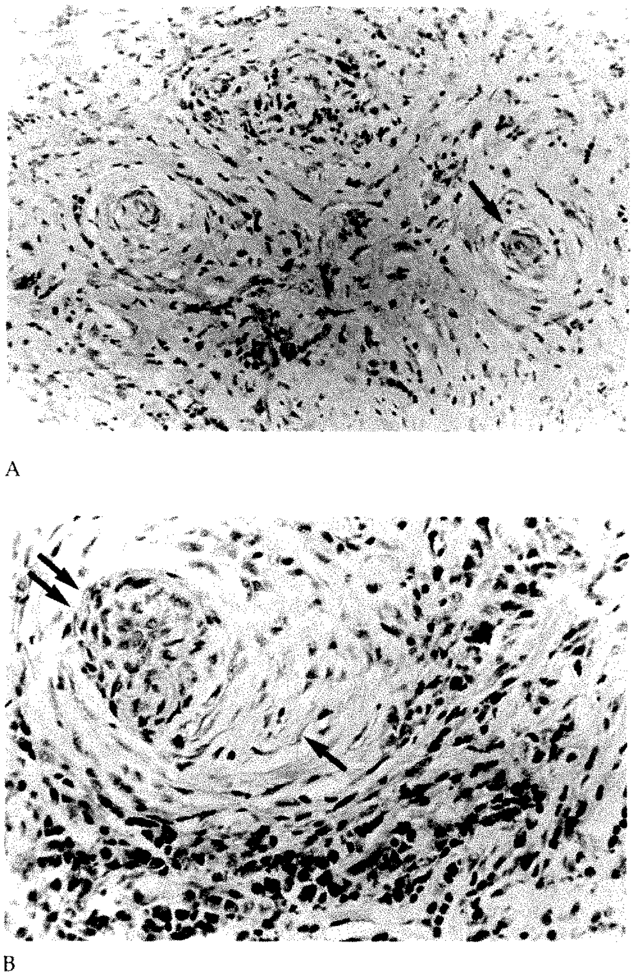


Fig 2. (A) Photomicrograph showing obliterative arteriolar changes (single arrow). *(B) Photomicrograph showing arteriolar medial thickening* (single arrow) *and intimal hyperplasia and obliteration* (double arrow)*; plasma cells and lymphocytes are seen in the perivascular areas.*

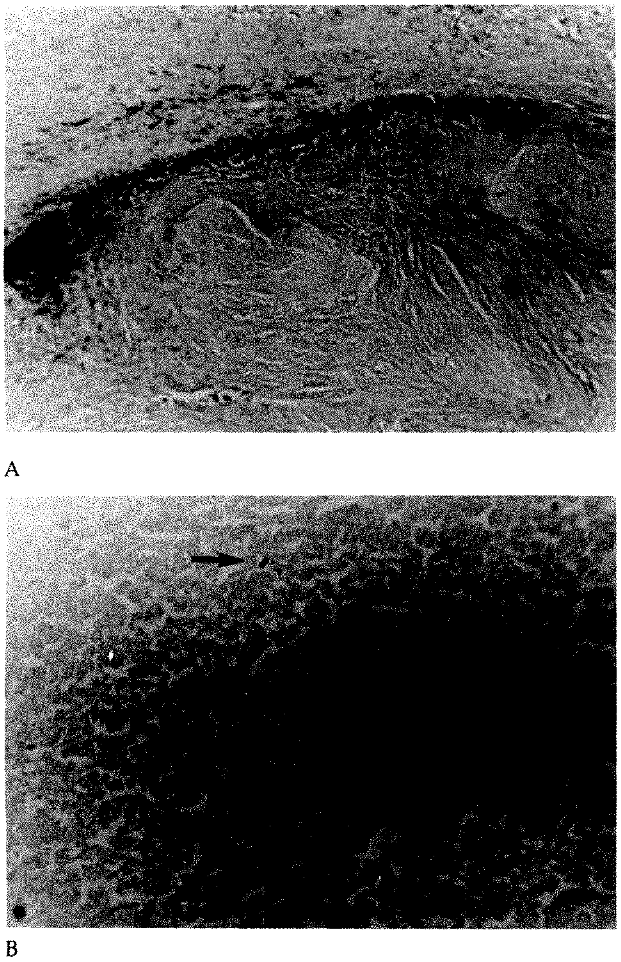


Fig 3. (A) Photomicrograph showing caseating granulomas. (B) Budding yeast forms demonstrated by silver stains (single arrow).

strated collateral circulation and often showed in delayed films the azygos vein as a source of collateral circulation. If bilateral brachial venograms could not be performed, an arch aortogram with follow-up visualization of the obstructed venous system on digital subtraction films was an excellent alternative. Cardiac catheterization was carried out in 3 patients. One patient demonstrated pulmonary artery compression with symptoms of shortness of breath, dyspnea on exertion, and hemoptysis. Two patients had pericardial involvement: one with bleeding and tamponade and the other with the postcardiotomy syndrome but both showing symptoms of shortness of breath, loss of energy, and pulsus paradoxus.

All patients had bronchoscopy and either cervical or second interspace mediastinoscopy. Care was taken in the mediastinoscopy procedure to avoid bleeding because of the increased collateral circulation. Washings and biopsy specimens were taken for cytological and bacteriological tests during the endoscopic procedures, and lymph node or mass biopsy specimens were taken through the mediastinoscope. Esophagoscopy was performed for patients with dysphagia. Complement fixation studies were drawn for histoplasmosis, coccidioidomycosis, and blastomycosis. Complement fixation titers of 1:32 or higher strongly suggested histoplasmosis. Although no specific titers were absolutely diagnostic, serial evaluation showing an increasing titer suggested an acute or subacute process in the fibrotic area, which was usually corroborated by an elevated sedimentation rate.

Retroperitoneal fibrosis occurred in 1 patient and has been associated with a common denominator of histoplasmosis. The patient was operated on initially with the diagnosis of retroperitoneal fibrosis, and the ureters were decompressed. Subsequently, the diagnosis of sclerosing mediastinitis was established, and histoplasmosis was incriminated. Ketoconazole controlled the symptoms without major surgical resection, and the patient has remained asymptomatic for 4 years.

Therapy

Two patients were seen with failure of surgical decompression, one of the trachea and the other of multiple bypass procedures for SVCO. An active process was diagnosed as secondary to histoplasmosis, and treatment of the histoplasmosis with ketoconazole successfully relieved the symptoms in both patients. Subsequently, 4 other patients with a diagnosis of sclerosing mediastinitis found to be secondary to histoplasmosis as evidenced by elevation of the serum of complement fixation levels and sedimentation rate were successfully treated with ketoconazole without the necessity of operative surgical bypass procedures or decompression.

Tracheal decompression was successfully accomplished in 2 patients with median sternotomy in 1 and a right lateral thoracotomy in the other. Two other patients, 1 of whom had both esophageal and tracheal decompression, underwent right lateral thoracotomy for esophageal decompression. Another patient who had major compression of his pulmonary arteries was decompressed bilaterally through a median sternotomy incision [22] and had a right middle lobectomy for chronic infection and obstruction of this lobe secondary to the obstructive process. One patient had division of a tracheoesophageal fistula secondary to granulomatous erosion with excellent preparation for operation by using esophageal diversion and exclusion [23]. Decompression of cardiac tamponade with partial pericardiectomy was performed in 1 patient. Postcardiotomy syndrome was diagnosed clinically in another patient who underwent medical therapy.

Superior Vena Caval Obstruction

Superior vena caval bypass or reconstruction was carried out in 6 of the 13 patients with SVCO. A wide variety of surgical procedures was used, the first being a Teflon graft from the innominate vein to the right atrium that remained open for more than 5 years as demonstrated by an angiogram. The patient remained asymptomatic during that time. In another patient, an aortic homograft bypass graft was inserted from the SVC to the right atrium and gave temporary relief, but symptoms recurred weeks later suggesting occlusion of the bypass graft. Three patients were treated with saphenous veins sutured together around a glass rod creating a composite concentric

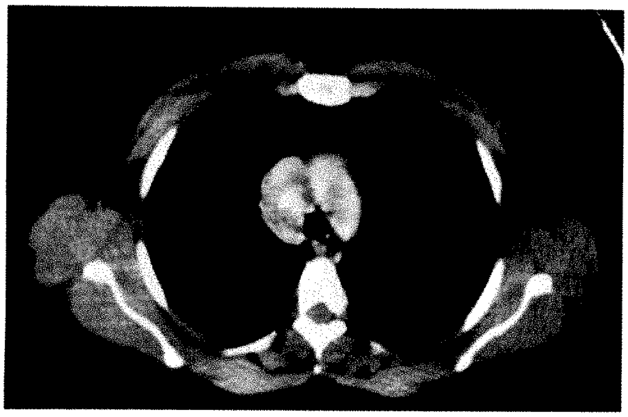


Fig 4. Computed tomographic scan showing mass compressing mediastinal structures, trachea, and esophagus.

graft that was inserted from the innominate vein to the right atrium. All three procedures were successful for a time range of 2 to 12 years. One patient underwent a direct anastomosis of the azygos vein and the inferior vena cava that provided bypass of the SVCO. This remained patent for 1 year.

Pivotal Clinical Cases

A 32-year-old woman was observed to have tracheal stridor accentuated on lying down and to have intermittent cyanosis and progressive dysphagia with marked weight loss for more than 2 months. She underwent bronchoscopy and esophagoscopy, which showed external compression of the trachea and esophagus (Fig 4). After cervical and second interspace mediastinoscopy failed to provide a diagnosis, median sternotomy with decompression of the trachea and esophagus and multiple biopsies of tissues were performed. It appeared as if someone had "poured concrete" into the superior mediastinum. There was no evidence of granuloma, carcinoma, or lymphoma, and the patient was subsequently treated symptomatically.

However, the patient was admitted 6 months later with shortness of breath, large mediastinal masses similar to those associated with lymphosarcoma, and evidence of pericardial tamponade (Fig 5). She required a left lateral thoracotomy with pericardiectomy and removal of a large hematoma, which produced decompression of the heart. No organisms were seen on the histological stains and on cultures. However, the complement fixation titer for histoplasmosis was 1:128, and the sedimentation rate was 85 mm/h. She was started on ketoconazole therapy of 400 mg daily. In 3 months, her chest roentgenogram returned to normal (Fig 5C). She has been asymptomatic for 8 years and has demonstrated remarkable clinical improvement. The dosage of ketoconazole therapy was gradually reduced in 1 year. Symptoms returned but disappeared promptly after restarting ketoconazole.

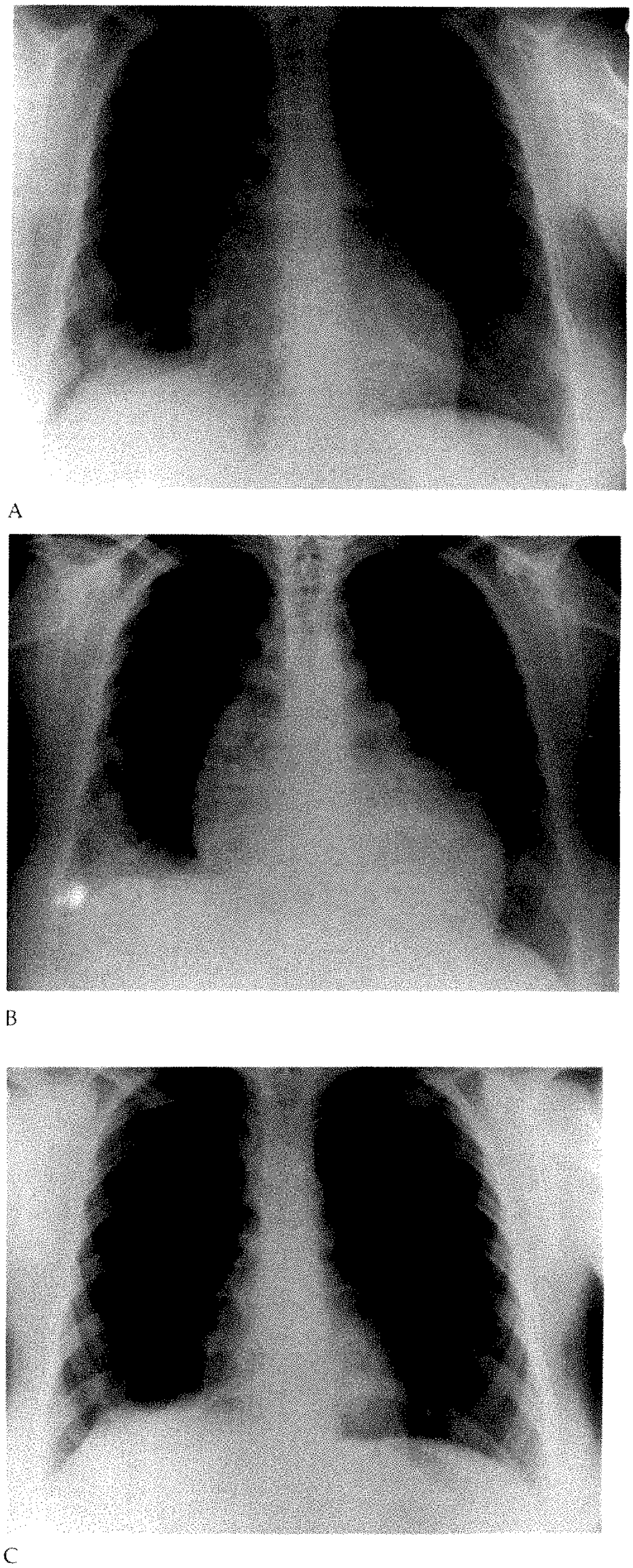


Fig 5. Chest roentgenograms. (A) Postoperative decompression. (B) Recurrent enlarging mediastinal masses 6 months later. (C) After ketoconazole treatment.

In a second 38-year-old patient, SVCO was diagnosed approximately 8 years previously. She had four superior vena caval reconstructions and bypass procedures over a period of 4 years. The initial operation involved decompression of the SVC and the mediastinum. This helped her for approximately 1 year, after which time recurrent symptoms developed. At this time she was reexplored and decompressed, and a composite saphenous vein bypass graft was placed from the innominate vein to the right atrium with amelioration of symptoms again for almost 1 year. Recurrent symptoms appeared when the vein graft occluded. At this time, the patient underwent decompression and an anastomosis between the azygos vein and the inferior vena cava, which palliated her symptoms for about a year (Fig 6). A percutaneous balloon angioplasty was carried out subsequently with only modest relief of the SVC stenosis (Fig 7) and symptoms, and the patient was readmitted after a fifth operation was recommended. She had an elevated sedimentation rate of 97 mm/h and an elevated complement fixation titer for histoplasmosis of 1:128. She was placed on ketoconazole therapy of 400 mg daily, and she had remission of her symptoms for approximately 4 years without evidence of any severe problem.

Subsequent to these 2 patients, 4 other patients have been evaluated with SVCO after biopsy that failed to show carcinoma. Each patient had elevated sedimentation rates and complement fixation levels of more than 1:64, and they were all treated successfully with ketoconazole. When ketoconazole therapy was stopped in 1 patient because of hepatitis of unknown cause, the SVCO symptoms recurred and again were ameliorated when ketoconazole was restarted.

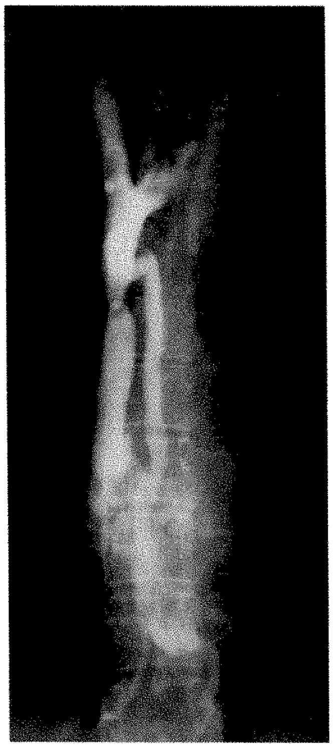
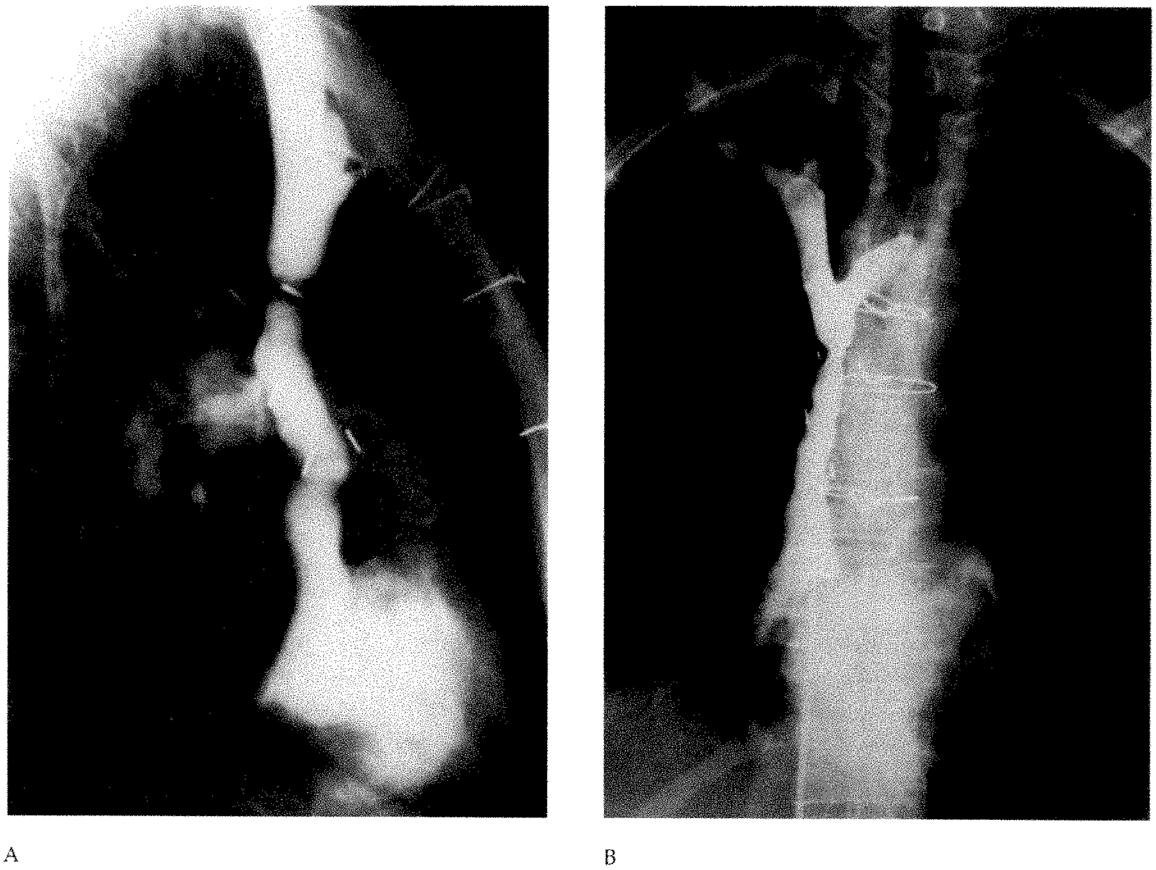


Fig 6. Venogram demonstrating azygous to inferior vena cava anastomosis for palliation of superior vena caval obstruction.



A B

Fig 7. Venograms. (A) Superior vena caval obstruction before percutaneous transluminal coronary angioplasty. (B) After percutaneous transluminal coronary angioplasty.

Comment

Sclerosing mediastinitis in most patients appears to be a self-limited process. Symptoms of SVCO should regress as collateral circulation evolves secondary to the obstruction over a period of weeks. Areas such as the trachea, esophagus, and even the pulmonary artery and veins when decompressed should remain patent if the process is self-limited.

In the patients with SVCO who have had multiple decompressive procedures and yet experience recurrent symptoms an active or subacute process is suspected that obstructs collateral circulation as it develops. This appears to be the situation in our series of patients who were evaluated by sedimentation rate and by histoplasmosis complement fixation titer and who demonstrated a regression of recurrent symptoms with the use of an antihistoplasmosis drug such as ketoconazole. In several patients, the symptoms would disappear with the ketoconazole and then reappear after its cessation. On reinstitution of the ketoconazole, the symptoms would again disappear. This directly proportional relationship between symptoms, elevated sedimentation rate, complement fixation titer, and drug therapy strongly suggests a subacute or chronic smoldering process of the sclerosing disease.

This same process occurred with compression of the trachea in 1 patient and the esophagus in another in which surgical decompression was followed by recurrent symptoms that were associated with an elevated sedimentation rate and complement fixation titers for histoplasmosis. With the use of ketoconazole, the symptoms were alleviated, and the sedimentation rate and the complement fixation titer for histoplasmosis were diminished. The same pattern evolved as with SVCO in that as soon as the medication was stopped, the symptoms recurred and then disappeared with reinstitution of ketoconazole.

There is no fixed duration for use of the medication in any given patient. Arbitrarily, a treatment period of 1 year has been used after the cessation of symptoms. After tapering the drug dosage, the clinical symptoms, the sedimentation rate, and the complement fixation titer for histoplasmosis are carefully monitored to determine whether or not to reinstitute the drug.

A corollary of these observations is that in patients with benign sclerosing mediastinitis secondary to histoplasmosis, a trial of ketoconazole may be indicated if the symptoms are not life-threatening before the surgical decompression of either the SVC or vital organs. If the patients became asymptomatic on the medical treatment alone, a major surgical intervention may be averted.

The side effects of ketoconazole have been minimal. One patient on several medications had a mild impairment of liver function requiring cessation of all drugs. However, in this patient ketoconazole administration was restarted at an interval phase because of symptom recurrence. Amelioration of the recurrent symptoms resulted with no liver toxicity.

The high incidence of histoplasmosis as an etiological factor in our particular series may represent the geographic patient referral pattern of our practice. Patients from Dallas and east of Dallas or from the Mississippi River drainage basin are highly susceptible to histoplasmosis.

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DISCUSSION

DR MARCUS L. DILLON, JR (Lexington, KY): This is an interesting group of patients who are terrible to take care of. I think it reinforced my impression about ketoconazole and its effectiveness with systemic histoplasmosis. The only way you can evaluate this is the recurrence rate, and I think you are running close to 100%. Amphotericin has only about a 10% recurrence rate in a year. It is referred to as "ampho-terrible" by the medical people, because we treated 190 patients with amphotericin at a hospital for patients with fungal infections and only 1 child was not able to tolerate it. My point is that I think amphotericin is a much more effective primary treatment for systemic mycoses.

DR JAMES W. PATE (Memphis, TN): I enjoyed very much Dr Urschel's usual very dramatic and definitive treatment of this disease. There is one thing that worries me about it though. You said there were 19 patients with histoplasmosis, but you did not give us any proof. You remember the paper we presented at the Southern Surgical Association meeting many years ago in which we first demonstrated a correlation between caval obstruction and histoplasmosis. The organism was rarely recovered from the mediastinum or from the lymph nodes; the only place from which we could recover the organism with any consistency was the lung granuloma. You did not mention any biopsy specimens from the lung, and you did not give us the serological titers. Did the titer go up when the patients got worse? Did it go down when they were treated? Was there any evidence of fluctuating titers that would assure us that they really did have histoplasmosis?

DR F. G. PEARSON (Ontario, Canada): I wish to ask Dr Urschel about the duration of therapy and the levels of complement titer abnormality that would prompt him to initiate therapy. We have had a similar experience in terms of the cross-section of patients with sclerosing mediastinitis. We identified histoplasmosis in about half of our patients. The other half remained idiopathic. No organisms were seen or cultured. No patients were treated with ketoconazole, nor have any of our patients been treated with amphotericin. We were dealing with burned-out disease, and we never considered that there could be any active, ongoing fungal infection. We thought it was a response to caseous material escaping from the nodes.

A number of patients have chronic upper airway obstruction not amenable to operation. In such patients I assume you recommend that we do the titers. At what point would you recommend treatment? My other question relates to duration of treatment. I sense you have had 1 or 2 patients on treatment for prolonged periods, measured in years.

DR URSCHEL: Proceeding in a retrograde order: I think the tracheal compression requires surgical intervention. You have to intervene anyway to look for a diagnosis, and I think to wait for a medical treatment on tracheal problems would be a mistake. The superior vena cava compression is just the opposite. You ought to treat it medically if you have assured yourself there is no malignancy present. Any titer over 1:32 we consider high. Any single titer measurement is not in itself diagnostic but only suggestive. Serial titer elevation confirms disease activity and dictates therapeutic management. In our experience, the titers have been extremely helpful in these 6 cases we are discussing. The last 6 of 6 cases have been histoplasmosis that we have documented. Doctor Pate, only 2 patients demonstrated organisms and positive cultures. All the rest were related to a rising histoplasmosis complement fixation titer and then a positive response to treatment.

Ketoconazole is a second-line drug, which is weaker than amphotericin B but can be taken by mouth. If one draws a line between Dallas and Ft Worth, everybody living to the west will usually have coccidiomycosis and everybody to the east will have histoplasmosis. We are not treating a systemic process as much as a localized process, and ketoconazole is a drug patients can take by mouth and can stop and start easily.

Patients with SVCO or the recurrent tracheal stenosis have frightening symptoms. If operation by good surgeons fails in a small percentage of cases, this subacute active process should be considered because most of these patients should either have development of a collateral circulation or get better with an operation if no active process is present.

Use of Potentially Infected Donor Hearts for Cardiac Transplantation

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Despite the nationwide shortage of heart donors, more patients, some of whom are critically ill, are being accepted as candidates for transplantation. Thus, on occasion, we have liberalized our donor criteria to meet the demand. We have recently transplanted 16 potentially infected donor hearts into critically ill recipients. Of these 16 donors, 7 had multiple positive blood cultures as follows: *Streptococcus pneumoniae* (3), *Staphylococcus aureus* (2), *Klebsiella pneumoniae* (1), and *Enterobacter* sp (1). Seven other donors were accepted despite high fevers (rectal temperature >38.9°C), leukocytosis (>18 × 10^9/L [>18,000 cells/μL]), and pulmonary infiltrates with positive sputa (*Enterobacter* [3], *Klebsiella pneumoniae* [2], and *Staphylococcus* [2]). Two other donors with hepatitis B surface antigen positivity were deemed at high risk but were used because the recipients were in immediate need. Early mortality (≤30 days) among the recipients was 3/16 (18.7%) with 1 patient dying of uncontrolled allograft rejection, 1 of hepatic failure, and 1 of *Pseudomonas* septicemia. Late mortality (>30 days after operation) occurred in 6 patients: 2 patients died of hepatic failure, 3 died of graft atherosclerosis, and 1 died of iatrogenic hemorrhage after a liver biopsy. Only 1 patient died of infection unrelated to that of the donor, and the other patients had no infectious complications resulting from the organisms identified in their respective donors. Use of potentially infected donor hearts resulted in surprisingly few infectious complications in this group of recipients. This practice can be safe and should be considered when other options are unavailable.

(Ann Thorac Surg 1990;50:222–5)

Cardiac transplantation has evolved into an accepted treatment for patients with end-stage cardiac disease, with a number of factors contributing to the general success of this treatment. These factors include selection of recipients according to definite criteria [1], improved techniques of acquisition and transport of the donor heart, improved tissue typing of both the donor and recipient, advances in perioperative management of the cardiac allograft recipient, employment of serial endomyocardial biopsies to diagnose rejection, and better protocols for achieving and monitoring effective immunosuppression. With the increase in the number of cardiac transplant centers, however, donor availability has become a major problem, and approximately 30% of the candidates die while awaiting a donor heart [2]. One feasible approach to alleviate this problem is to liberalize donor criteria.

Many potential donors who are otherwise healthy are rejected because they test positive for various types of infection, a well-known threat to recipients who require chronic immunosuppression. Infection continues to be a major cause of morbidity and mortality in cardiac transplant patients [3, 4] despite immunosuppressive protocols that have been developed to reduce the risk of disease transmission and surveillance of the donor and the harvested organ for bacterial and viral organisms. Even with these precautions, some patients receive organs from donors later known to have been infected, and, occasionally, if a candidate is critically ill, transplantation is undertaken even when such facts are known prospectively. This report examines our data involving the use of potentially infected donor hearts and suggests, from the lessons we have learned, how patients who have such hearts might be managed.

Material and Methods

The hospital records and follow-up donor charts of 320 cardiac transplant recipients operated on at the Texas Heart Institute between July 1982 and September 1989 were reviewed. Both orthotopic and heterotopic transplant recipients were included, and all patients received cyclosporine-based immunosuppression according to our specific protocols regarding age and renal function [5]. Of the 320 patients, 16 (5.0%) received hearts from potentially infected donors defined as follows: multiple (>2) positive blood cultures (7 patients); leukocytosis (>18 × 10^9 L [>18,000 cells/μL]) in conjunction with positive sputa, pulmonary infiltrates, and a rectal temperature >38.9°C (7 patients); or the serologic presence of hepatitis B surface antigen (HBsAg) (2 patients). All 16 patients were in the intensive care unit at the time of transplantation and required various inotropic and chronotropic

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supportive agents. In 5 (31%) of the patients, intraaortic balloon counterpulsation was also required. Prophylactic broad-spectrum antibiotics were given to all patients preoperatively and were continued until chest tubes and central venous lines were discontinued. In addition, pathogen-specific antibiotics were administered preoperatively and continued 7 to 10 days postoperatively. Donor hearts were assessed at the procurement site for the presence of valvar vegetations, myocardial abscesses, or frank pus.

The mean age of the donors was 25 years (range, 11 to 42 years), and the causes of death included neurologic injuries in 12 patients, multiple trauma in 3, and a drug overdose in 1. The average time from the occurrence of fatal trauma to the donor cardiectomy was 87 hours (range, 24 to 336 hours). The recipient group comprised 12 men and 4 women with a mean age of 43 years (range, 11 to 65 years). Only 2 (12%) of the recipients were insulin-dependent diabetics, and 4 (25%) were cytomegalovirus-negative.

All donor pathogens were known preoperatively. Seven patients received hearts from bacteremic donors, including *Streptococcus pneumoniae* (3), *Staphylococcus aureus* (2), *Klebsiella pneumonia* (1), and *Enterobacter* sp (1). Seven patients received hearts from patients with suspected pneumonia with sputa positive for *Enterobacter* sp (3), *K pneumoniae* (2), and *S aureus* (2). Two other critically ill patients in immediate need received hearts from HBsAg-positive donors, with one recipient receiving hepatitis B immunoglobulin preoperatively. All 16 recipients and, whenever possible, their donors received antibiotics specific for the cultured organism. All patients underwent orthotopic heart transplantations.

Serial endomyocardial biopsies were obtained at weekly intervals and graded according to the McAllister scale [6]. Episodes of rejection were treated with either intravenous cyclosporine, corticosteroid pulses, or muromonab-CD3 (Orthoclone OKT_3) monoclonal antibody. Members of the Infectious Diseases Department served as consultants in coordinating the surveillance and treatment of any infections. All central-line catheters were removed after 7 days, or sooner if fever occurred, and a new site was chosen if further central venous access was required.

Results

Of the 16 cardiac transplant recipients who received potentially infected donor hearts, 6 experienced advanced rejection (endomyocardial biopsy score ≥ 7) within 90 days of transplantation, but opportunistic infection (*Pneumocystis carinii*) developed in only 1 patient. No recipients became infected with or died of the pathogen identified in their respective donors.

Three recipients died early in the postoperative period (range, 18 to 28 days), and all had received hearts from donors with positive blood cultures: 2 with *S pneumoniae* and 1 with *S aureus*. The causes of death in these patients included drug-induced hepatic failure, uncontrolled rejection (in a patient with a retrospectively positive crossmatch), and *Pseudomonas* septicemia that began in the urinary tract. Initial immunosuppression varied among these 3 recipients with 1 each having received cyclosporine and prednisone; cyclosporine, prednisone, and azathioprine; and OKT_3 and prednisone.

Late deaths (>30 days after transplantation; range, 33 days to 4.5 years) occurred in 6 patients whose donors had positive sputa (3), positive blood cultures (2), and presence of HBsAg (1). The causes of late deaths included graft atherosclerosis (3), hepatic failure (2), and iatrogenic hemorrhage after a liver biopsy in 1 of the HBsAg-positive-donor patients. (The biopsy results were negative for hepatitis.) Neither recipient receiving an HBsAg-positive donor heart developed serologic evidence of hepatitis B (range of follow-up, 33 days to 2.5 years).

Follow-up for all patients averaged 1.6 years (range, 18 days to 4.5 years). Among survivors, the lack of infectious complications specific to the donor heart pathogen has continued. Chronic maintenance immunosuppression consists of cyclosporine and corticosteroids in all survivors. Postoperative left ventricular ejection fractions in these recipients have been similar to those of all other cardiac transplant recipients at our institution, averaging 0.54 and 0.55 at 3 and 12 months, respectively.

Comment

Preventing infection in the immunosuppressed allograft recipient remains a fundamental goal of the transplantation strategy. Protocols including bacteriological surveillance of both the donor and the harvested organ have been developed to reduce the risk of disease transmission. Historically, when pertinent cultures were positive, the allograft was not used for transplantation.

This report describes our experience with prospectively recognized cardiac donor infections, most of which were bacterial. Although at least one report has urged caution in such situations [7], we were stimulated to proceed with transplantation despite the potential for infection, at least initially, by the lack of suitable donor hearts for some of our critically ill recipients. Untreated, donor-transmitted bacterial infections have been reported to cause anastomotic disruptions in renal transplant recipients [8], but this had not been described in cardiac recipients. We were cautiously optimistic that, in this instance, the benefits of expanding our donor pool would outweigh the risks involved. The surprisingly good results obtained to date will hopefully stimulate others to study the issue in an effort to further define the limits of safe practice.

Concern for the risk of donor-to-recipient transmission of human immunodeficiency virus (HIV) grows as transplant-related cases are reported and the number of asymptomatic, potentially infected carriers increases. Reports suggest that between 0.3% [9] and 7% [10] of potential organ donors are seropositive for HIV, and any donor shown to have antibodies is believed to harbor a transmissible virus [11]. Human immunodeficiency virus infection can develop in transplant patients in two ways: exogenous infection transmitted by way of an HIV-seronegative donor allograft or by way of donor blood transfusions, and transplantation performed in an asymptomatic HIV-positive recipient. There is evidence that primary infections with HIV from the donor organ can occur during the course of transplantation [12, 13] and that the first episode of severe opportunistic infection in the presence of a positive antibody test can be seen as early as 4 months and as late as 3 years after transplantation [14]. The actual timing of the phlebotomy for the HIV test may further mislead the transplant surgeon, as the massive blood transfusions that are common to trauma patients, some of whom become donors, can yield a false-negative result owing to dilution [15].

The problem of performing transplantation in an HIV-seropositive recipient is less clear. Some reports provide evidence that this group of recipients suffers a high mortality from infection because the disease itself induces immunosuppression [16, 17]. Other studies in liver transplant recipients suggest that the survival of HIV-positive recipients is essentially no different from that of recipients known to be negative [9]. Although it may be premature to make HIV infection an absolute contraindication to cardiac transplantation, our current approach is not to use HIV-positive donors or to perform transplantation in HIV-positive recipients until the issues are more clear. The specter of acquired immunodeficiency syndrome in the transplant population is very real, and we advise professional caution on both philosophical and practical grounds.

Another life-threatening infection seen in cardiac transplant recipients is toxoplasmosis. Although reactivation of latent infections with immunosuppressive agents is certainly possible, in most cases *Toxoplasma gondii* is transmitted by transplanting a seropositive donor's heart into a seronegative recipient [18, 19]. The diagnosis can be difficult, as involvement of the donor myocardium by toxoplasmosis interferes with the assessment of rejection. The infection may produce a mononuclear cellular infiltrate that mimics lymphocytic rejection activity, thereby suggesting the need for increased immunosuppression. Our present approach is to serologically screen both donor and recipient for toxoplasmosis. If a recipient was seronegative before transplantation and converts after receiving a seropositive donor heart, prophylactic pyrimethamine is given, and this maneuver has been shown to be effective [20].

Cytomegalovirus (CMV) is a major cause of morbidity and mortality in cardiac transplant recipients and has frequently been linked to rejection, graft atherosclerosis, and death [21]. As the prevalence of seropositivity for the CMV antibody in the general population is approximately 40% to 45% [22], the cardiac donor shortage would be compounded by avoiding donors with positive CMV titers. Fortunately, primary CMV infections are associated with considerably greater morbidity and mortality than are simple reactivations. The use of polyvalent intravenous immunoglobulin has been shown to be beneficial in modifying the severity of CMV infections and in preventing interstitial pneumonias after allogeneic marrow transplantation [23]. As part of our routine preoperative evaluation, all patients are screened for prior exposure to CMV. Patients who are CMV-negative are given screened blood free of CMV antibodies. Cytomegalovirus-negative recipients who receive a CMV-positive heart are not treated for infection, even if they seroconvert, unless an overwhelming CMV infection develops.

Transplanting donors with HBsAg positivity has been reported to produce equivocal success rates in renal transplant patients. The presence of HBsAg in kidney recipients apparently affects neither graft nor patient survival up to 2 years after transplantation [24], but it may have an unfavorable effect on long-term survival [25]. In neither one of our recipients with hepatitis-positive donors did HBsAg positivity develop on subsequent serologic studies. One recipient did receive hepatitis-B immunoglobulin at the time of transplantation, but we currently do not have a standard protocol for such patients. We do not recommend using hepatitis-positive donors for heart transplantation unless the prospective recipient is critically ill and death is imminent. If HBsAg is detected retrospectively in the donor, our current plan is not to treat the recipient unless problems occur.

In conclusion, our study suggests that recipients can have safe transplants from donors having noncardiac bacterial infections, although the number of patients is too small to make either specific or lasting recommendations. We can state that if one of our prospective recipients is critically ill and using a heart from an infected donor appears to be the only (or best) option, we will proceed with transplantation. Although the principle may seem unsound, this strategy has worked well in practice. Until the donor shortage dilemma is resolved or more effective means are devised for treating end-stage cardiac disease, the cautious expansion of donor criteria will be necessary. The practice of accepting potentially infected donor hearts for transplantation creates surprisingly few infectious complications in the recipients, can be safe, and should be considered when other options are unavailable.

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DISCUSSION

DR WILLIAM A. BAUMGARTNER (Baltimore, MD): This is a topic that is somewhat controversial, as are all of the ways to increase the number of donors. I think part of the key to accepting donors with systemic infection is the time from which the diagnosis was made and antibiotics were started. How long were the donors treated before cardiectomy was performed in the patients who had bacteremia?

My second question revolves around another extension of donor criteria, and that is the age at which one accepts donor hearts. I noticed that in the late deaths, 3 of the 6 patients died of graft atherosclerosis, and that has been linked in the past to an older-aged donor. Were these patients in whom graft atherosclerosis developed older than the traditionally accepted donor age of 35 years?

DR LAMMERMEIER: The majority of the donors were noted to be on pathogen-specific antibiotics once bacteremia was diagnosed. If not, they were placed on antibiotics once our transplant coordinators were notified of such a potential donor. The majority of bacteremic donors were placed on antibiotics for approximately 48 hours prior to cardiectomy. All recipients were administered preoperative pathogen-specific antibiotics, which were continued 7 to 10 days postoperatively.

The 3 recipients who died as a result of graft atherosclerosis received hearts from donors less than 40 years of age.

DR SAFUH ATTAR (Baltimore, MD): I think in our enthusiasm to treat sick patients, we forget that the means will not justify the end or the end will not justify the means. I am sure you have considered the ethical and legal problems involved in this aspect. I would be interested to know what were your deliberations before you accepted taking infected hearts and using them as donors.

DR LAMMERMEIER: The idea of using hearts from infected donors was not considered in our early transplant experience. However, when approximately 30% of our transplant candidates died because of donor organ shortage, we began accepting potentially infected donor hearts in select cases. Thus far, although our series is small, the strategy has worked well, and we continue to consider the use of such donors for candidates when no other options are available.

Severe Aortic Stenosis in Octogenarians: Is Operation an Acceptable Alternative?

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From 1981 to 1989, 60 patients more than 80 years of age were referred for operation for severe calcific aortic stenosis. All patients were symptomatic: 13 in New York Heart Association (NYHA) functional class II, 28 in class III, and 19 in class IV. The preoperative mean cardiothoracic ratio was 0.58 ± 0.09; the mean valve area, 0.52 ± 0.14 cm^2; and the mean aortic valve gradient, 62 ± 18 mm Hg. Left ventricular function was impaired in 30 patients (ejection fraction < 0.40). Coronary arteriography was performed in 10 patients. Aortic replacement used bioprosthesis in all 60 patients associated with aortocoronary bypass (in 5) and mitral valve replacement (in 1). One-month mortality rate was 28% (17 patients) due to cardiac failure (in 9), pulmonary complications (in 6), and neurological complications (in 2). Early mortality was not correlated with preoperative angina, cardiothoracic ratio, associated operation, and cross-clamping time. It was not obviously correlated with preoperative functional class but correlated positively with urgent operations and with left ventricular function (40% mortality in patients with ejection fraction < 0.40 versus 16% mortality in others). Hospital morbidity was 68%. Mean hospitalization was 15 ± 7 days. There were four late deaths. Thirty-nine patients are long-term survivors (3 months to 7 years): 27 in class I, 10 in class II, and 2 in class III due to primary valve failure. The actuarial survival probability is 65% at 1 year and 61% at 5 years. In summary, the good long-term quality of life justifies the high postoperative risk in octogenarians. Early operation before cardiac function impairment improves the results.

(Ann Thorac Surg 1990;50:226–9)

In the past 10 years, cardiac operation in patients more than 70 years of age has become a routine procedure, and a number of reports have been published on the higher but acceptable perioperative mortality and morbidity rate in this select population [1–6]. Patients more than 80 years old are now frequently referred to cardiac surgeons. However, few papers so far have focused their attention on octogenarians, who show more controversial results than those of septuagenarians in term of feasibility [7–9].

This report describes our experience with open heart operation in 60 octogenarians referred homogeneously over an 8-year period to an aortic valve replacement for severe calcific aortic stenosis. Predictive factors of early mortality and morbidity are discussed, and indications are identified as tolerable-risk and high-risk patients.

For editorial comment, see page 173.

Material and Methods

Aortic valve replacement in patients more than 80 years of age have been performed since the middle of 1981 in our institution, and this series concerns 60 patients operated on up to July 1989. Anesthesiological protocol was the same throughout this period, extracorporeal circulation was performed with a membrane oxygenator, and myocardial protection used cold crystalloid cardioplegia solution added to topical cooling. In all patients, a biological valve was implanted: 44 pericardial valves (Mitroflow in 26, Carpentier-Edwards in 10, Sorin Pericarbon in 6, and Ionescu-Shiley in 2), and 16 porcine valves (Wessex in 8, Hancock in 6, Liotta in 2). An associated procedure was performed on 6 patients: a single venous bypass graft on the left anterior descending coronary artery in 4, a double venous bypass graft on the left anterior descending and right coronary arteries in 1, and a mitral valve replacement by bioprosthesis in 1.

Data included patient age and sex, admitting diagnosis and clinical symptoms, New York Heart Association (NYHA) functional class, cardiothoracic ratio on chest roentgenography, renal function, echographic or angiographic evaluation of left ventricular function, and coronary arteriography if performed. Aortic cross-clamping time was recorded. Postoperative course was followed up in terms of bleeding, cardiac and renal status, assisted ventilation duration, and neurological events. Early mortality was defined as death within 30 days of the initial procedure.

Follow-up information from the cardiologists was obtained on all 60 patients, and was added to the patients' physical examination performed by surgeons when these patients were still alive.

Data are presented as mean ± standard deviation.

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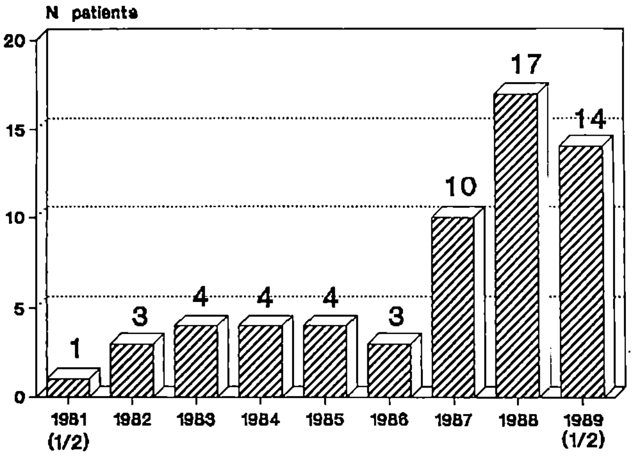

Fig 1. Annual activity of aortic valve replacement for severe aortic stenosis in octogenarians through an 8-year period.

Statistical comparisons among preoperative and postoperative factors were made by χ^2 test for discrete variables or by Student's t test for continuous variables, and the significance level chosen was $p < 0.05$. Actuarial survival of the 60 patients was calculated by the Kaplan-Meier method.

Results

Among the 60 patients, 27 were male and 33 were female (age range, 80 to 88 years; mean, 82 ± 3). The number of operations performed every year was small until 1986, then increased considerably after that time; its percentage of the overall activity in our department went from 0.3% in the first 6 years to 2% in 1988 (Fig 1). All patients had severe calcific aortic valve stenosis confirmed at the time of operation. Mean aortic valve area was 0.52 ± 0.14 cm^2 and mean left ventricle–aorta gradient was 62 ± 18 mm Hg. Preoperative major symptoms are shown in Table 1. Thirteen patients were in New York Heart Association class II; 28, in class III; and 19, in class IV. From the latter group, 6 patients underwent operation on an emergency basis, defined as immediate operations in hemodynamically unstable patients. Cardiothoracic ratio was more than 0.50 in all patients (range, 0.51 to 0.64; mean, 0.58 ± 0.09).

Left ventricular function was considered impaired when ejection fraction was less than 0.40 or shortening fraction was less than 0.22. Thirty patients responded to these criteria. A history of possible coronary disease was found in 25 patients, but a coronary arteriography was performed in only 10 patients (17%) leading to an associated coronary gesture in 5 patients (8.5%) as previously mentioned. The small number of coronary arteriographies was related to many cardiologists' reluctance in proposing such a procedure to very old patients with evident signs of severe aortic stenosis. Six patients had a previous balloon aortic valvoplasty followed by an immediate restenosis.

Preoperative renal function was considered good for these patients of advanced age when plasma creatinine level was less than 120 µmol/L (1.4 mg/dL). Forty-three patients were in this criteria. Seventeen patients had some type of renal insufficiency (creatinine level, 120 to 226 µmol/L [1.4 to 2.6 mg/dL]). The operations were performed with a mean aortic cross-clamping time of 77 ± 23 minutes (range, 46 to 159 minutes).

Early death occurred in 17 patients (28%). Nine patients died of a cardiac cause; 5, of myocardial incompetence with immediate death (2 in the operating room who could not come off bypass); and 4, of major sudden irreversible rhythm disorder in the following days. Six patients died of a pulmonary cause with prolonged assisted ventilation followed by multivisceral failure. Two patients died of a neurological reason: 1 was unconscious at the time of operation and never recovered, and the other had a stroke after 3 weeks.

As predictive factors of early mortality, no statistical significance could be pointed out concerning preoperative proportion of angina or syncope, preoperative distribution of cardiothoracic ratio (0.59 ± 0.04 in early-death group versus 0.57 ± 0.05 in survivors), preoperative coronary arteriography, duration of aortic cross-clamping time (77.2 ± 20 minutes in early-death group versus 76.9 ± 25 minutes in others), or the existence of an associated surgical procedure; two early deaths (33%) occurred among the 6 patients with combined procedures. Preoperative renal dysfunction showed a trend toward being a bad prognosis factor (creatinine level 126 ± 48 µmol/L [1.4 ± 0.5 mg/dL] in early-death group versus 106 ± 30 µmol/L [1.2 ± 0.3 mg/dL] in survivors), but the level of statistical significance was not reached ($p = 0.08$). Among the 17 patients in the early-death group, 47% were in preoperative class IV, 35% were in class III, and 18% were in class II; but no statistical significance could be pointed out compared with the early-survival group in which 26% of the patients were in class IV, 51% were in class III, and 23% were in class II. However, operation on an emergency basis seemed to indicate a bad prognosis as 10% of the 60 patients were in this preoperative criteria and 30%

Table 1. Major Preoperative Findings in the 60 Octogenarians Who Underwent Aortic Valve Replacement

Variable	No. of Patients	Percentage (%)
Symptoms		
Angina	43	72
Syncopa	16	27
Functional class[a]		
IV	19	32
III	28	47
II	13	21
Risk factors		
Smoking	7	12
Hypertension	13	21
Diabetes	6	10
Obesity	6	10

[a] New York Heart Association.

of the early-death group were urgent cases ($p < 0.01$). Early mortality was 40% in the group of 30 patients with impaired left ventricular function and 16% in the remaining 30 patients with better left ventricular function. This difference was significant ($p < 0.05$). Furthermore, it is interesting to note that early mortality was 35% in patients operated on before 1988, which significantly differed from 19% mortality in people operated on after 1988 ($p < 0.05$).

Hospital morbidity occurred in 41 patients (68%) with prolonged low cardiac output in 13 patients (11 patients had an impaired preoperative left ventricular function), pulmonary edema in 11, acute renal insufficiency in 9, and pulmonary sepsis in 8. Thirty-five percent of the patients had assisted ventilation for more than 24 hours postoperatively. Two patients (3.3%) returned to the operating room for excessive bleeding. Seventeen patients (28%) had postoperative atrial fibrillation medically treated. Mean duration of hospitalization for survivors was 15 ± 7.5 days, which was about 4 days more than the usual overall mean time spent in our department. One patient had prolonged hospitalization (3 months) owing to sternal wound infection.

Four late deaths were recorded: one, at 4 months in a woman whose general condition worsened progressively because of anorexia and who died of cachexia; two, at 14 months and 4 years, because of irreversible chronic cardiac failure; and one caused by breast cancer 5 years after the operation.

Among the 39 long-term survivors (3 months to 7 years), all are ambulatory; 27 are in functional class I and 10 are in class II (Fig 2). Two patients, 87 and 85 years of age, are in class III because of primary valve failure of their biological prosthesis at 18 and 70 postoperative months, respectively. Some problems were encountered in the long-term survivors such as the need for pacemaker implantation (1), the need for operation for hip prosthesis (1) or angina (2), medically treated breast cancer (1), and some type of temporospatial disorientation requiring psychiatric treatment (2). The overall actuarial survival curve shows a 65% survival rate at 1 year and a 61% survival rate at 5 years, which 5 patients of this series have passed (Fig 3).

Comment

Cardiac operation in patients more than 70 years of age has been widely documented [1–6]. Perioperative mortality has ranged from 3% to 50% in the different series, the high deviation being explained by differences in selection of the patients and type of cardiac operation, as well as changes in myocardial protection in the period of report publication [2, 10]. The risks have been considered to be acceptable in these septuagenarians, with a worse prognosis in patients who had valve replacement (especially mitral valve replacement) and in patients who had emergency operation, were in preoperative class IV, had renal dysfunction, and had impaired left ventricular function [1, 4, 6, 11–13].

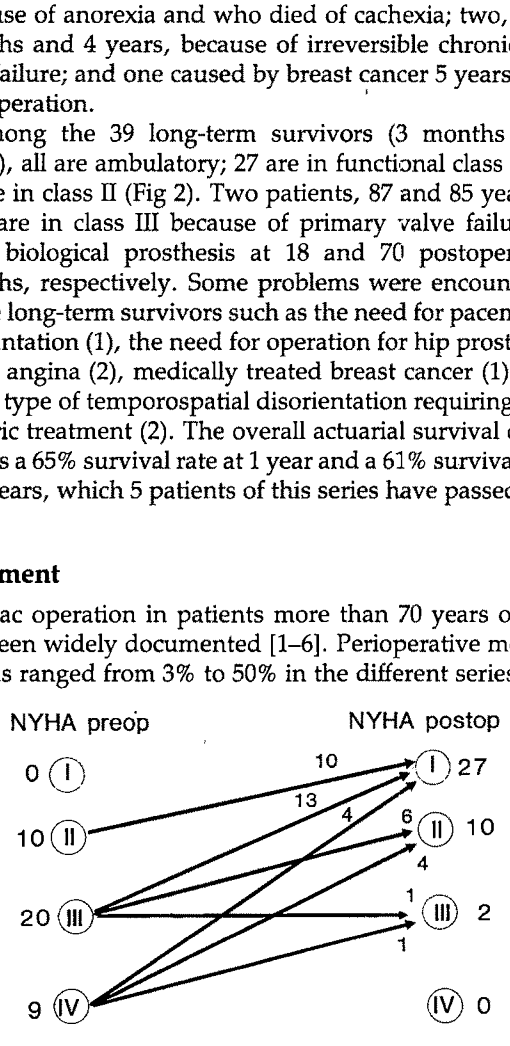

Fig 2. Preoperative and postoperative New York Heart Association (NYHA) classification functional status of 39 long-term survivors.

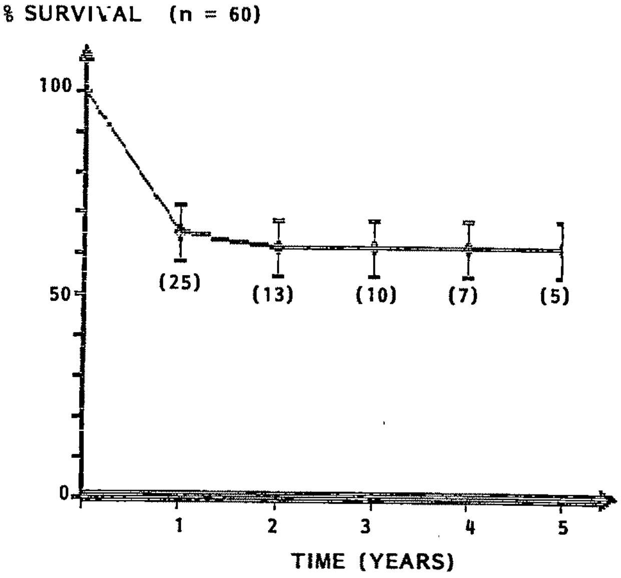

Fig 3. Actuarial survival curve for the 60 patients with vertical bars *showing standard errors. The numbers in parentheses below the curve denote patients at risk.*

Few reports have focused their data on patients more than 80 years old. The earlier reports published small numbers of cases [7], and the more recent works gathered a wide variety of cardiac surgical procedures [8, 14, 15]. The present series is one of the biggest reported so far on octogenarians referred for a similar cardiac surgical procedure in a relatively small period of time [9]. Sixty patients underwent an aortic valve replacement for severe calcific aortic stenosis over an 8-year period. Early mortality was 28%, which is comparable with the series of operations performed by Edmunds and co-workers [8] on patients including those at high risk. This mortality rate was highly correlated with the emergency of the operation and with the preoperative left ventricular function status. Six patients were treated on an emergency basis, and 5 of them died early. Fifty percent had preoperative left ventricular function impairment, and early mortality was 40% in this group compared with 16% early mortality in the group with good left ventricular function. Furthermore, growing experience in selection and management of octogenarians in our experience led to a significant decrease to 10% in the past year's early mortality rate [7, 9, 14, 15]. Patients in preoperative functional class IV and with renal dysfunction showed a trend toward a greater early mortality rate, but this difference did not reach the level of statistical significance as it did in other studies [10, 13] probably because of insufficient number of patients reported here.

Hospital morbidity in this series was unusually high (68%) as compared with routine cardiac operations. This figure is observed in all series on patients with advanced age [7–9]. The most striking remark is the small number of patients with neurological events (8%) compared with patients with cardiac (30%), pulmonary (45%), and renal (22%) complications [7]. Five patients had nevertheless some type of encephalopathy, all but 2 recovered in a variable period of time through the first month. Incidence of sternal wound infection (3.3%) and of immediate postoperative bleeding requiring reoperation (3.3%) was not higher than in current open heart operations. Contrary to other reports [3], hemorrhagic complications during follow-up were not a problem as most of the living patients (91%) could be weaned from anticoagulation therapy; the main reason for this was the use of a biological prosthesis in all patients.

Long-term quality of life and survival rate are particularly encouraging and might justify by themselves the acceptability of open heart operation in octogenarians. The survival is comparable with the general survival curve of unselected octogenarians with "normal" life [16] and, most of all, the benefit of the operation is tremendous because 70% of the survivors are in class I, 25% are in class II, and all living patients find a subjective improvement. One point has to be noted. The 2 patients in class III had a malfunctioning bioprosthesis by primary valve failure after 18 and 70 months (one porcine valve, one pericardial). As far as anticoagulation is concerned, the use of a bioprosthesis in octogenarians is recommended [4, 6, 11, 17], but will lead to the problem of therapeutic management of primary valve failure in patients more than 85 years of age!

Balloon aortic valvoplasty has been proposed as an alternative to operation in the treatment of aortic valve stenosis [18]. Nevertheless, published hospital mortality ranged from 3% to 10% [19–21], and hospital morbidity was from 10% to 25%. Furthermore, immediate restenosis (within 72 hours) occurred in 25% of patients, and 66% had restenosis within 6 months [21]. Finally, actuarial survival curves showed less than 80% survival at 1 year, and functional improvement did not occur in all patients.

In summary, it appears acceptable to propose an operation for severe aortic stenosis to octogenarians with unmanageable cardiac symptoms, preferentially before onset of left ventricular impairment.

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Preservation of Myocardial Function and Biochemistry After Blood and Oxygenated Crystalloid Cardioplegia During Cardiac Arrest

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We compared the ability of blood cardioplegia and oxygenated crystalloid cardioplegic solutions to maintain regional left ventricle contractility and adenosine triphosphate levels after cardiopulmonary bypass. Ten baboons were subjected to 90-minute cardiopulmonary bypass conducted at 28°C. Hemodynamic measurements were made before and after the bypass procedure, and biopsies for high-energy phosphate determinations were performed at different time intervals during and after bypass. The results showed improved maintenance of myocardial contractility (measured with the regional end-systolic pressure–length relationship) with the oxygenated crystalloid solution. Expressed as a percentage of values before bypass, contractility after bypass averaged 81.69% ± 4.81% and 80.47% ± 10.05%, respectively, after 10 and 20 minutes using the oxygenated crystalloid cardioplegia. For blood cardioplegia, the corresponding values were 71.9% ± 8.73% and 64.99% ± 8.60% (mean ± standard error of the mean). The 10- and 20-minute postbypass values between the two groups differed significantly (*t* test, Welch modification: $p = 0.0464$ and $p = 0.0342$). Myocardial adenosine triphosphate level was higher immediately after induction of cardiac arrest when blood cardioplegia was used (blood cardioplegia, 6.82 mol · g wet wt^{-1}; crystalloid cardioplegia, 4.95 mol · g wet wt^{-1}; $p = 0.0314$), but values subsequently equalized.

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The advantages of an oxygenated crystalloid cardioplegic solution during elective arrest are well established [1–3]. Similarly, use of blood cardioplegia (BC) is associated with excellent preservation of myocardial function after cardiopulmonary bypass procedures [4–7]. Although comparisons have been made between nonoxygenated crystalloid solution and BC [5, 6, 8], few studies have compared an oxygenated crystalloid solution with BC [7, 9]. The results were contradictory: some indicated that BC was superior to oxygenated crystalloid cardioplegia (OCC) [7], whereas others failed to demonstrate a difference [9, 10] in circumstances relevant to our clinical practice. None of the published information addressed the question of myocardial contractility using an independent index, however. Therefore, this study compared the efficacy of BC and OCC in preserving myocardial contractility in the first 20 minutes after the cardiopulmonary bypass period.

For editorial comment, see page 175.

Material and Methods

This study was approved by the Ethics Committee of the Faculty of Medicine of the University of Stellenbosch. The animals were cared for in accordance with national and institutional guidelines.

Ten baboons (*Chacma pupio ursinus*, weighing 25 to 30 kg) were used. Anesthesia was induced with intramuscular ketamine, 15 mg · kg^{-1}. The animals were intubated and mechanically ventilated with nitrogen (60%) and oxygen (40%) (Bird MK4, Bird Corp, Palm Springs, CA). The ventilatory frequency was kept constant at eight breaths per minute, and the tidal volume was varied to maintain the arterial carbon dioxide tension between 34 and 38 mm Hg. Anesthesia was maintained for the duration of the study with 0.5% halothane vaporized from a calibrated vaporizer (Ohmeda, England). Normal saline solution was infused at a constant rate of 5 mL · kg^{-1} (total volume, 250 mL) and the temperature, measured from the esophagus (Yellow Springs Instruments, Yellow Springs, OH), was maintained between 36.5° and 37.3°C with an undertable heating system.

A stiff 16-gauge catheter was inserted into the femoral artery and advanced into the aorta. This catheter was connected to a pressure transducer (AE 840, Horten, Norway) for determination of aortic pressure. Through one femoral vein, a 7F pulmonary artery catheter (American Edwards, Santa Ana, CA) was floated into the pulmonary artery (PA) and connected to a transducer similar to the first. This catheter and transducer recorded PA pressure and PA wedge pressure (PAWP). Cardiac output (CO) was obtained from a manual injection of 5 mL 5% cold dextrose for 4 seconds into the proximal port

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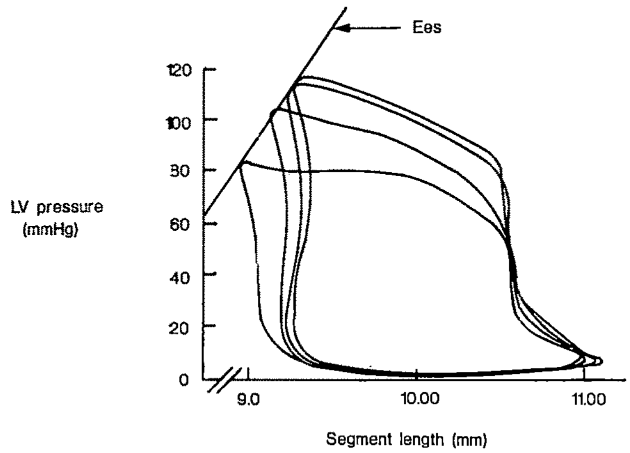

*Fig 1. The end-systolic pressure–length relationship (*Ees*) obtained from a number of subsequent beats in which the afterload was increased. The slope of the line Ees is an index of myocardial contractility.* (LV = *left ventricular.)*

of the PA catheter. A computer (Spectramed, Oxnard, CA) calculated the CO; the mean of three CO determinations is reported. The coefficient of variation for the 30 triplicate determinations was 2.4%. Through the other femoral vein, a central venous pressure (CVP) cannula was positioned in the right atrium. An occlusion catheter (Fogarty 81/14, Edwards Laboratories, Santa Ana, CA) was introduced into the femoral artery and positioned with its tip just above the diaphragm.

After the catheters were placed, a median sternotomy was performed and the pericardium was opened. A stiff catheter (8F) was sutured into the left ventricle apex, connected to a pressure transducer (AE840, Horten), and used for continuous registration of left ventricular (LV) pressure. During bypass, this cannula acted as an LV vent. Zero value for all pressure measurements was taken at the level of the LV apex.

Microsonometry was used to register regional myocardial dimensions [11]. Two piezoelectric crystals were implanted in the LV subendocardium, midway between the apex and base of the heart and approximately 1 cm lateral to the left anterior descending coronary artery. We attempted to position the crystals 1 cm apart to minimize the scatter of the recorded data. The signals from the crystals were recorded, processed (Schuessler and Assoc, Cardiff-by-Sea, CA), and displayed on an oscilloscope (Textronics, Guernsey, Channel Islands). The crystals registered the maximum segmental length at the end of diastole (just before the opening of the aortic valve) and the minimum segmental length at the time the aortic valve closed. The difference between maximum and minimum segmental length is segmental systolic shortening, and this could be normalized for maximum segmental length and expressed as a percentage. By combining the LV pressure signal and the segmental length changes, we registered a continuous pressure–length loop (Fig 1).

Aortic and mixed venous blood gases and hemoglobin (Hb) concentration were measured regularly before and during cardiopulmonary bypass (AVL Gas Check, Switzerland; BMS, Buffalo, NY; IL 143, Lexington, MA; Radiometer, Copenhagen, Denmark). Corrections were made when necessary to maintain the variables within the physiological range. Electrolytes were measured in arterial blood (SMAC 11, Technicon, England).

The animal was heparinized (3 $mg \cdot kg^{-1}$ heparin) through the central venous line, and venous (right atrial) and aortic cannulas were inserted. The animal was placed on cardiopulmonary bypass using a clear prime (in $mmol \cdot L^{-1}$: Na^+, 130; K^+, 4; Mg^{2+}, 3.0; Cl^-, 110; pH, 7.4; 273 $mosm \cdot L^{-1}$). A roller pump (Sarns 3750, Sarns, Ann Arbor, MI) delivered flow (70 to 90 $mL \cdot kg^{-1}$), which was adjusted to maintain the arterial pressure between 70 and 85 mm Hg for the duration of bypass. After partial bypass was established, the temperature of the animal was reduced to 28°C and was maintained for the duration of the bypass (105 ± 4.3 minutes).

Total bypass was instituted, and the left ventricle was emptied. When ventricular fibrillation occurred, the aortic cross-clamp was applied and the cardioplegic solution infused. The cross-clamp remained on the aorta for 90 minutes. After infusion of the designated volume of cardioplegic solution (described below), a transmural LV biopsy was taken with a modified dental drill [12]. The biopsy specimens were taken 1 cm superior and lateral to the segment from which the segmental lengths were recorded. The specimen was immediately stored in liquid nitrogen until extraction of high-energy phosphates. Analyses were done using a high-performance liquid chromatography technique as described previously [13].

At the end of bypass, the animal was rewarmed to 37°C and bypass was terminated. The cannulas were removed within 10 minutes after volume challenges were applied to restore the PAWP and CVP to approximate prebypass values. No inotropes, calcium, or protamine were administered.

The heart was allowed to function for 20 minutes once the cannulas were removed. Thereafter, the experiment was terminated with an injection of pentobarbital followed by KCl. The position of all the catheters was confirmed at postmortem examination.

Cardioplegic Solution

Two cardioplegic solutions were used (Table 1). Selection was made by a blind card draw, and each group consisted of 5 animals. Asystole was achieved with an infusion of 10 $mL \cdot kg^{-1}$ of the solution; during bypass, 5 $mL \cdot kg^{-1}$ of either solution was administered every 20 minutes at a constant pressure of 50 mm Hg through a closed system kept in ice. The temperature of the solution before entering the aortic root was approximately 4°C.

BLOOD CARDIOPLEGIA. Blood cardioplegia was constituted by mixing 250 mL of the animal's blood (after institution of bypass) with 250 mL of Plasmalyte B (Sabax, Johannesburg, South Africa). Ten millimoles of KCl was added to the initial solution, and 5 mmol was added to the subsequent solutions (5 animals).

Table 1. Composition of Cardioplegic Solutions[a]

Variable	Blood Cardioplegia	Oxygenated Crystalloid Cardioplegia
Temperature (°C)	4.20 ± 0.02	4.00 ± 0.01
Hb (g/dL)	4.49 ± 0.43	0.00
PO_2 (mm Hg)	332.62 ± 20.21	436 ± 20.2[b]
Na^+ (mmol/L)	132.42 ± 1.21	132.43 ± 1.40
K^+ (mmol/L)	25.1 ± 1.2 (8.21 ± 1.20)	23.5 ± 1.2 (7.28 ± 0.70)
Cl^- (mmol/L)	133 ± 2.21	129 ± 1.02
Ca^{2+} (mmol/L)	3.48 ± 0.20	1.18 ± 0.01[b]
Mg^{2+} (mmol/L)	1.16 ± 0.07	3.00 ± 0.02[b]
PO_4^{2-} (mmol/L)	0.45 ± 0.10	0.00
Albumin (g/L)	12.62 ± 0.70	0.00
HCO_3^- (mmol/L)	33.21 ± 2.21	43.02 ± 1.20[b]
pH	7.63 ± 0.01	7.38 ± 0.10

[a] Values are the mean ± standard error of the mean for all samples of a particular cardioplegic solution (n = 25). The value indicated for K^+ (outside parentheses) are values for the initial cardioplegia (n = 5). The values in parentheses are representative of all the subsequent doses (n = 20). [b] $p < 0.01$.

Ca^{2+} = calcium; Cl^- = chloride; Hb = hemoglobin; HCO_3^- = bicarbonate; K^+ = potassium; Mg^{2+} = magnesium; Na^+ = sodium; PO_2 = oxygen tension; PO_4^{2-} = phosphate.

OXYGENATED CRYSTALLOID CARDIOPLEGIC SOLUTION. Oxygenated crystalloid cardioplegic solution consisted of Plasmalyte B to which 20 mmol of KCl and 1.20 mmol of $CaCl_2$ was added. Oxygen (100%) was continuously bubbled through the crystalloid solution (5 animals).

Hemodynamic Measurements and Calculations

Measurements were taken after calibration and verification of the zero pressures. A microcomputer collected data directly, and sampling was performed at 200 Hz for 5 seconds, 10 seconds after the endotracheal tube was disconnected (zero airway pressure). Three measurements were made during the course of the experiment: M1, immediately before placement of the bypass cannulas; M2, 10 minutes after termination of the bypass and removal of the cannulas; and M3, 20 minutes after removal of the cannulas.

Apart from the primary pressure and CO recordings, the heart rate was calculated from the LV pressure signal. The end-systolic pressure (in mm Hg) is the LV pressure at the time the aortic valve closes.

The following calculations were performed on the primary data: Mean arterial pressure (MAP, in mm Hg) was calculated by the computer from the area under the aortic pressure recording. Mean pulmonary artery pressure (MPAP, in mm Hg) = (systolic PA pressure − diastolic PA pressure)/3 + diastolic PA pressure. Left ventricular stroke work (LVSW, in g · m) = 0.00136(MAP − PAWP) × stroke volume (SV). Right ventricular stroke work (in g · m) = 0.00136 (MPAP − CVP) × SV. Systemic vascular resistance (in dynes · s · cm^{-5}) = MAP − CVP × 80/CO. Pulmonary vascular resistance (in dynes · s · cm^{-5}) = MPAP − PAWP × 80/CO. Arterial oxygen content (CaO_2, in mL · 100 mL $blood^{-1}$) = (0.0139 × Hb × arterial oxygen saturation [SaO_2]) + (0.0031 × arterial oxygen tension). Mixed venous oxygen content ($C\bar{v}O_2$, in mL · 100 mL $blood^{-1}$) = (0.0139 × Hb × venous oxygen saturation [SvO_2]) + (0.0031 × arterial oxygen tension). Arteriovenous oxygen difference [$(a - \bar{v})O_2$, in mL · 100 mL $blood^{-1}$] = $CaO_2 - C\bar{v}O_2$. Oxygen consumption ($\dot{V}O_2$, in mL · min^{-1}) = CO × $(a - \bar{v})O_2$. Oxygen delivery (DO_2, in mL · min^{-1}) = CO × CaO_2.

END-SYSTOLIC PRESSURE–LENGTH RELATIONSHIP. Segmental myocardial contractility was quantified with the end-systolic pressure–length relationship, which was obtained from the pressure–length loop (Fig 1). The aortic occlusion balloon was used to increase the proximal aortic pressure over five to eight beats. This led to an increase in LV pressure. The computer recognized the maximum pressure–length ratio for each of the beats and then used these points in a linear regression (least-squares) calculation to determine the slope (Ees) and *x*-axis intercept; Ees is an index of regional myocardial contractility [14–16]. By simple mathematical manipulation, the segment length at the time of zero LV pressure could be calculated. This is represented as the intercept of Ees on the length axis (in millimeters). Regional LV work was obtained from the area under the pressure–length loop [17].

MYOCARDIAL ADENOSINE TRIPHOSPHATE. Transmural LV drill biopsy specimens were taken for determination of tissue adenosine triphosphate (ATP) [13] at the following times: immediately after asystole was achieved and initial infusion of the cardioplegic solution (B1); 30 minutes after the initial biopsy (B2); 60 minutes after the initial biopsy (B3); 90 minutes after the initial biopsy (B4); and 20 minutes after cardiopulmonary bypass was terminated and the cannulas were removed (after registration of the final hemodynamic data and before termination of the experiment (B5).

Table 2. Myocardial Adenosine Triphosphate Concentrations[a]

		ATP Concentration ($\text{mol} \cdot \text{g wet weight}^{-1}$)	
Biopsy	Time	Blood Cardioplegia	Oxygenated Crystalloid Cardioplegia
B1	After cardiac arrest	6.82 ± 0.44	4.95 ± 0.82[b]
B2	30 min after arrest	6.55 ± 0.70	6.74 ± 1.42
B3	60 min after arrest	5.03 ± 0.89	5.51 ± 1.45
B4	90 min after arrest	4.98 ± 0.52	4.07 ± 1.02
B5	20 min after termination of bypass	4.56 ± 1.32	4.48 ± 0.32

[a] Values are the mean ± standard error of the mean. Statistical analysis was performed between blood and oxygenated crystalloid cardioplegia. [b] $p < 0.05$.

ATP = adenosine triphosphate.

Statistical Analysis

The unpaired t test was applied when the two groups were compared, and the α value was prospectively set at 0.05. If, however, the variances differed significantly, the Welch modification of the t test was used [18]. Normality was checked; if the residuals were appreciably nonnormal, the Wilcoxon rank-sum test was applied.

For comparison of data from a single group, repeated-measures analysis of variance was used. If the F value indicated a significant difference, specific differences were sought with the Student Newman-Keuls test.

Results

Control Values

Comparison of the values obtained at M1 failed to demonstrate any differences between the two groups except for the ATP concentration, which was significantly higher in the BC group ($p = 0.0314$) (Table 2).

Blood Cardioplegia

The following variables showed significant change (Tables 3, 4): MAP, $F = 5.18$ and $p = 0.0174$; Hb, $F = 20.48$ and $p = 0.0001$; $(a - \bar{v})O_2$, $F = 4.77$ and $p = 0.029$; $S\bar{v}O_2$, $F = 4.20$ and $p = 0.030$; and venous oxygen tension ($P\bar{v}O_2$), $F = 4.21$ and $p = 0.022$.

The MAP decreased from M1 to M2 ($p = 0.029$) and from M1 to M3 ($p = 0.0071$). No difference was observed between M2 and M3. The Hb level decreased from M1 to M2 ($p = 0.0004$) and from M1 to M3 ($p = 0.0008$).

The $(a - \bar{v})O_2$ decreased from M1 to M2 ($p = 0.013$) and from M2 to M3 ($p = 0.0071$). There was no difference between M1 and M3. The $S\bar{v}O_2$ decreased from M1 to M2 ($p = 0.010$) and M3 ($p = 0.007$), and a similar tendency was demonstrated for $P\bar{v}O_2$ ($p = 0.011$, $p = 0.032$).

Although there was a tendency for the myocardial ATP content to decrease during the course of the experiment, the changes were not significant ($F = 1.110$, $p = 0.396$).

Oxygenated Crystalloid Cardioplegia

The following variables differed significantly (see Tables 3, 4): systemic vascular resistance, $F = 5.76$ and $p = 0.018$; $S\bar{v}O_2$, $F = 4.58$ and $p = 0.033$; and Hb, $F = 6.33$ and $p = 0.013$.

Specific measurement times analysis showed that the Hb level decreased from M1 to M2 ($p = 0.016$) and from M1 to M3 ($p = 0.005$). M2 and M3 did not differ. The systemic vascular resistance decreased from M1 to M2 ($p = 0.017$) and from M1 to M3 ($p = 0.33$). Again there was no difference between M2 and M3. The $S\bar{v}O_2$ decreased from M1 to M2 ($p = 0.025$) and from M1 to M3 ($p = 0.033$). M2 and M3 did not differ. Adenosine triphosphate concentration remained unchanged ($F = 1.213$, $p = 0.345$)

Comparison of Blood Cardioplegia and Oxygenated Crystalloid Cardioplegia

Values of Ees failed to indicate significant differences between M2 and M3 (Table 5, Fig 2). (M2, Welch modification, "effective" degrees of freedom = 4.868 and $p = 0.584$; M3 values, $p = 0.295$.) When Ees was expressed as a percentage of M1 (prebypass control) $[(M_2 - M_1)/M_1 \cdot 100]$, significant differences could be demonstrated between M2 ($p = 0.0464$) and M3 values ($p = 0.0342$). Comparison of the values of the intercept of Ees on the length axis failed to demonstrate a difference (M2, $p = 0.377$; M3, $p = 0.20$). The values of $P\bar{v}O_2$ and $(a - \bar{v})O_2$ were significantly less in the BC group at 20 minutes after bypass as compared with the OCC group ($p = 0.030$ and 0.018, respectively) (see Table 4).

Comment

There is still a paucity of data comparing OCC with BC, and in this study we operated from the assumption that (1) myocardial contractility is equally well preserved when either BC or OCC is used during elective hypothermic arrest; and (2) there is no difference in the function of the heart as a pump (ie, the ability to maintain supply of oxygen [CO × CaO_2] commensurate with oxygen con-

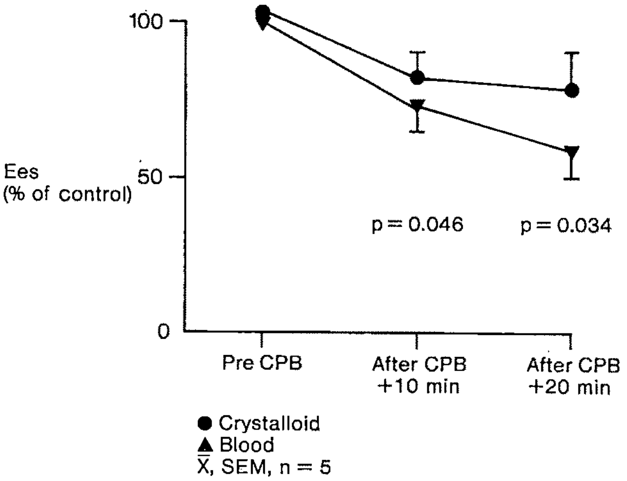

Fig 2. The normalized end-systolic pressure-length relationship (Ees) before and after cardiopulmonary bypass. The p values indicate the difference between blood and oxygenated crystalloid cardioplegia. (CPB = cardiopulmonary bypass; SEM = standard error of the mean.)

Table 3. General Hemodynamics Before and After Bypass[a]

Solution	HR (beats/ min)	MAP (mm Hg)	MPAP (mm Hg)	CVP (mm Hg)	LVEDP (mm Hg)	CO (L/min)	SV (mL)	SVR (dynes · s · cm^{-5})	LVSW (g · m)	PVR (dynes · s · cm^{-5})	RVSW (g · m)	dP/dt$_{max}$ (mm Hg/s)
Crystalloid cardioplegia												
M1, prebypass (control)	75.60	92.20	14.87	2.30	11.60	2.13	28.24	3,412.10	31.50	130.47	4.82	1,716.95
	± 1.29	± 7.87	± 1.57	± 0.20	± 1.29	± 0.16	± 2.27	± 287.02	± 4.73	± 30.73	± 0.81	± 328.10
M2, postbypass (10 min)	94.40	71.53	17.67	3.25	13.40	2.60	27.86	2,109.12	21.80	132.03	5.38	1,615.49
	± 7.03	± 7.71	± 1.30	± 0.63	± 1.29	± 0.13	± 1.59	± 236.71[b]	± 2.61	± 21.86	± 0.27	± 432.87
M3, postbypass (20 min)	90.00	72.80	16.87	2.44	12.40	2.12	23.92	2,678.89	19.27	159.67	4.67	1,936.67
	± 8.67	± 7.70	± 0.91	± 0.66	± 1.03	± 0.14	± 1.34	± 289.97[c]	± 1.61	± 45.50	± 0.37	± 597.16
Blood cardioplegia												
M1, prebypass (control)	94.74	85.20	14.87	3.47	12.00	2.04	22.02	3,260.04	22.79	128.26	3.59	1,202.80
	± 5.61	± 5.95	± 0.87	± 0.65	± 1.96	± 0.14	± 2.85	± 184.33	± 4.76	± 17.22	± 0.35	± 205.69
M2, postbypass (10 min)	88.80	67.07	15.73	3.73	12.00	2.41	27.35	2,287.02	20.33	139.84	4.64	1,362.96
	± 5.32	± 4.83[b]	± 1.31	± 0.90	± 1.54	± 0.30	± 3.72	± 356.11	± 3.02	± 44.07	± 0.48	± 317.38
M3, postbypass (20 min)	81.60	63.80	15.13	3.20	10.20	2.01	25.46	2,621.49	18.52	168.98	4.32	1,591.40
	± 6.25	± 3.25[b]	± 0.81	± 0.33	± 1.47	± 0.29	± 4.97	± 336.96	± 3.69	± 60.49	± 0.69	± 182.51

[a] Values are the mean ± standard error of the mean for 5 animals. Statistical analysis was performed between control value (M1) and each of the postbypass values (M2, M3). [b] $p < 0.05$; [c] $p < 0.01$.

CO = cardiac output; CVP = central venous pressure; dP/dt$_{max}$ = maximum rate of pressure increase; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVSW = left ventricle stroke work; MAP = mean arterial pressure; MPAP = mean pulmonary arterial pressure; PVR = pulmonary vascular resistance; RVSW = right ventricle stroke work; SV = stroke volume; SVR = systemic vascular resistance.

Table 4. Blood Gases, Oxygen Consumption, and Hemoglobin Concentration Before and After Elective Cardiac Arrest[a]

Solution	PaO_2 (mm Hg)	SaO_2 (%)	$PaCO_2$ (mm Hg)	pH	$P\bar{v}O_2$ (mm Hg)	$S\bar{v}O_2$ (%)	Hb (g/dL)	$(a-v)O_2$ (mL/100 mL)	$\dot{V}O_2$ (mL/min)
Crystalloid cardioplegia									
M1, prebypass (control)	205.40 ± 42.87	99.48 ± 0.19	36.03 ± 2.07	7.42 ± 0.04	39.80 ± 2.56	82.94 ± 1.42	13.18 ± 1.30	6.99 ± 0.69	144.65 ± 3.14
M2, postbypass (10 min)	165.60 ± 43.54	99.48 ± 0.19	36.08 ± 2.85	7.40 ± 0.04	39.60 ± 3.97	70.46 ± 4.21[b]	9.10 ± 0.76[d]	6.59 ± 0.73	167.95 ± 11.78
M3, postbypass (20 min)	157.00 ± 29.27	99.48 ± 0.16	36.03 ± 5.06	7.41 ± 0.02	38.20 ± 4.76	73.76 ± 2.78[b]	8.20 ± 1.02[d]	5.60 ± 0.69	166.56 ± 12.21
Blood cardioplegia									
M1, prebypass (control)	241.60 ± 31.45	99.70 ± 0.36	36.00 ± 0.51	7.40 ± 0.01	40.80 ± 2.80	78.40 ± 1.20	13.28 ± 0.76	8.46 ± 0.95	172.49 ± 23.49
M2, postbypass (10 min)	229.40 ± 29.98	99.80 ± 0.16	36.80 ± 2.87	7.41 ± 0.01	33.80 ± 2.08	69.86 ± 3.60[b]	7.82 ± 0.52[d]	7.72 ± 0.54[d]	185.84 ± 29.14
M3, postbypass (20 min)	234.60 ± 35.01	99.70 ± 0.21	36.60 ± 0.51	7.38 ± 0.02	31.80 ± 2.48[b,c]	64.20 ± 5.19[b]	8.46 ± 0.67[b]	8.68 ± 0.78[b,c]	173.01 ± 26.58

[a] Values are the mean ± standard error of the mean. [b] $p < 0.05$ versus control. [c] $p < 0.05$ versus oxygenated crystalloid cardioplegia. [d] $p < 0.01$ versus control.

$(a\text{-}v)O_2$ = arterial-venous oxygen difference; Hb = hemoglobin; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension; $P\bar{v}O_2$ = mixed venous oxygen tension; SaO_2 = arterial oxygen saturation; $S\bar{v}O_2$ = mixed venous oxygen saturation; $\dot{V}O_2$ = oxygen consumption.

Table 5. Regional Myocardial Mechanics in Animals Receiving Blood Cardioplegia or Oxygenated Crystalloid Cardioplegia[a]

Solution	P_{es} (mm Hg)	L_{max} (mm)	dL (mm)	Ees (mm Hg · mm)	Ees% (%)	Regional SW (mm Hg · mm)	L_o (mm)
Crystalloid cardioplegia							
M1, prebypass (control)	87.48 ± 5.43	15.12 ± 1.53	2.22 ± 0.21	101.30 ± 4.07	100.00 ± 0.00	195.43 ± 25.87	10.42 ± 0.82
M2, postbypass (10 min)	67.90 ± 7.90	14.85 ± 1.09	1.96 ± 0.21	81.30 ± 9.09	81.69 ± 4.81	134.83 ± 25.19	11.54 ± 0.96
M3, postbypass (20 min)	68.10 ± 5.68	14.46 ± 1.14	1.86 ± 0.14	79.66 ± 8.78	80.47 ± 10.05	126.96 ± 16.01	11.85 ± 0.97
Blood cardioplegia							
M1, prebypass (control)	72.86 ± 5.94	13.34 ± 1.90	2.27 ± 0.44	104.14 ± 18.93	100.00 ± 0.00	172.09 ± 46.34	10.15 ± 1.23
M2, postbypass (10 min)	61.00 ± 7.66	13.35 ± 2.14	2.54 ± 0.33	72.14 ± 15.07	71.19 ± 8.73[b]	160.21 ± 33.46	8.84 ± 2.39
M3, postbypass (20 min)	41.04 ± 11.08	12.29 ± 2.98	2.05 ± 0.33	59.58 ± 15.94	64.99 ± 8.60[b]	98.74 ± 32.86	7.25 ± 2.72

[a] Values are the mean ± standard error of the mean for five animals. [b] $p < 0.05$ versus oxygenated crystalloid cardioplegia.

dL = segmental shortening; Ees = end-systolic pressure-length relationship; Ees% = Ees percentage; L_{max} = end-diastolic segment length; L_o = x-axis intercept of Ees; P_{es} = end-systolic pressure; regional SW = regional stroke work.

sumption) after operative cardiac arrest and use of BC or OCC.

A previous study [9] evaluated the effect of red blood cells and calcium added to OCC and showed that addition of calcium to the cardioplegic solution was required to sustain myocardial performance after arrest. Red blood cells did not contribute to maintenance of myocardial performance over and above the benefit derived from calcium [9]. The study of Heitmuller and colleagues [9] measured myocardial function with maximum rate of pressure increase and LV function curves, however. The rate of pressure increase during the isovolemic phase of the cardiac cycle and LV function curves are load-dependent qualities [14]. Although Heitmuller and colleagues [9] controlled the LV end-diastolic pressure in an attempt to eliminate changes in preload, the nonlinear relationship between LV end-diastolic pressure and volume does not allow use of LV end-diastolic pressure as an absolute indication of preload. Furthermore, the LV afterload (LV wall stress or arterial impedance) was not controlled, and possible changes in afterload conditions make interpretation of the data in the study of Heitmuller and colleagues [9] difficult.

To overcome the abovementioned problems with measurement of myocardial function, we used the end-systolic pressure–length relationship (Ees) as an index of regional myocardial contractility. Previous studies have shown that this index is sensitive in defining changes in regional myocardial contractility and is not affected by the preload or afterload [15, 16, 19, 20]. It must, however, be emphasized that the Ees measures regional function as opposed to the end-systolic pressure–volume relationship, which is used to quantify global myocardial function [14]. The load-independent character of the Ees makes it particularly useful when the preload and afterload cannot be measured or if loading conditions cannot be controlled between experimental steps.

Evaluation of the Ees failed to demonstrate differences in regional myocardial contractility after hypothermic arrest when BC or OCC was used. When the data were transformed and expressed as a percentage of the control (prearrest value) to allow for individual differences in the initial measurement, however, results indicated that myocardial contractility was better maintained in hearts receiving OCC. Furthermore, it appears that the downward trend in Ees for the BC group had a tendency to continue, whereas the Ees in the OCC group remained at a stable (depressed) value. This observation will require further study, however.

Myocardial contractility refers only to the inherent ability to perform work for a given set of circumstances. This potential for delivering blood flow is modified by the heart rate, preload, and afterload experienced by the ventricles. The performance of the heart as a pump relates to delivery of an output (and oxygenated blood) that will satisfy the oxygen requirements of the body and hence sustain aerobic cellular respiration [21]. Although myocardial contractility per se is important, we cannot measure it in clinical practice and it is therefore often overshadowed by the necessity to maintain an efficient circulation. The latter can be measured at the bedside, and it is a fairly simple matter to manipulate the flow by adjusting the loading conditions of the heart. In addition, preload and afterload adjustment, within certain constraints, can often overcome the effects of a poorly contracting myocardium.

To judge the maintenance of cellular oxygenation, the $P\bar{v}O_2$ is used. [22, 23]. Cellular oxygenation represents the balance between O_2 supply and demand, and the factors involved can be discussed with reference to the rearranged Fick equation, which states that $C\bar{v}O_2 = CaO_2 - \dot{V}O_2/CO$. Because of the linear relationship between the $C\bar{v}O_2$ and $P\bar{v}O_2$ in venous blood, $C\bar{v}O_2$ reflects cellular oxygenation [23] provided that the $\dot{V}O_2$ is intact. The postbypass $P\bar{v}O_2$ in the OCC group did not change from prebypass values. In the BC group, however, the postbypass values at both 10 and 20 minutes were significantly lower than the prebypass values. The $P\bar{v}O_2$ value of 31.80 ± 2.48 mm Hg at 20 minutes after bypass is indicative of a moderate mismatch between oxygen supply and demand [22]. This deduction is supported by the significant increase in oxygen extraction ($[a\text{-}v]O_2$) in the BC animals, which contrast with the constant extraction values measured in the OCC group.

We cannot fully explain these differences. The CaO_2 and CO were of similar magnitude for both groups. The $\dot{V}O_2$ consistently tended toward higher values in the group receiving BC but did not reach statistical significance. Conceptually, it is also difficult to predict why the postbypass $\dot{V}O_2$ should differ between the BC and OCC groups because only the hearts were exposed to the cardioplegic solution. Similarly, changes in the P_{50} probably would not explain the difference in $P\bar{v}O_2$ because a similar blood acid–base control was used for both groups during bypass. It is possible that the difference in $P\bar{v}O_2$ can be explained by differences in CO but our sample was too small to demonstrate such a difference.

The ATP concentration at the initial biopsy (immediately after the aortic cross-clamp was applied and the heart fibrillated and after the initial cardioplegia was administered) was higher in the group receiving BC. The better oxygen-carrying characteristics of BC at the higher temperature probably were responsible for this. Cognizance must be taken of the fact that at the time of the first biopsy myocardial temperature still was higher than the eventual temperature once the bypass was established and the cold cardioplegia was infused. The transient lowering of the ATP level in the OCC group at the initial biopsy resulted from the interaction of incomplete cooling of the heart, myocardial fibrillation, and the limited oxygen-carrying capacity of the clear fluid. As the heart was cooled, however, this initial difference disappeared, and our results suggest that the oxygen contained in the OCC was sufficient to meet the oxygen demand in the cold-arrested myocardium, which supports results of previous studies [1, 10].

In summary, our data rejected our null hypothesis that no difference exists in the ability of the OCC and BC to maintain myocardial contractility and the integrity of the circulation after bypass and hypothermic arrest. Results indicate that in our model OCC resulted in better myocardial performance. Furthermore, provisional analysis suggests that it would be advantageous to arrest the heart with a blood-containing cardioplegic solution; thereafter OCC can be used.

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Myocardial Protection by Retrograde Cardioplegia in Arterial Switch Operation

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Retrograde coronary sinus perfusion of cold cardioplegic solution was evaluated in infants undergoing an arterial switch operation for transposition of the great arteries. To assess myocardial injury during ischemia, hemodynamic measurements were conducted at weaning from cardiopulmonary bypass and a postoperative assay of creatine kinase isoenzyme MB was performed. In 22 infants with retrograde coronary sinus perfusion, the initial cardioplegic infusion was performed through the aortic root and additional infusion was repeated every 30 minutes by retrograde coronary sinus perfusion. The other 11 infants received additional solution by antegrade selective coronary artery perfusion. The aortic cross-clamp time in the retrograde coronary sinus perfusion group was significantly shorter than that in the antegrade selective coronary perfusion group (128 ± 19 versus 145 ± 21 minutes, $p < 0.05$). There were no significant differences between the two groups in terms of postoperative hemodynamic variables and enzyme indexes. Eight neonates in the retrograde coronary sinus perfusion group also exhibited enzymatic and hemodynamic indexes similar to those of the older infants. These results suggested that retroperfusion of cardioplegic solution was a safe and useful means of myocardial protection in infants and neonates because of the simplification of the operative procedure and the avoidance of traumatic injury to the coronary ostia.

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The technique of retrograde coronary sinus perfusion (RCSP) has been reported to be a simple and beneficial method of cardioplegic delivery in adult patients undergoing either aortic valve operations [1] or coronary artery bypass grafting [2]. We successfully adopted this cardioplegic delivery technique in more than 70 infants undergoing anatomical repair for transposition of the great arteries (TGA) with a low surgical mortality of 4% [3]. Because this operative procedure consists mainly of coronary ostial transfer and switching of the great arteries, direct coronary cannulation is required to ensure antegrade cardioplegic delivery during ischemia. Selective coronary artery perfusion not only may produce traumatic damage to the coronary ostium [4], however, but also may complicate the operative procedure by requiring coronary ostial cannulation.

The present study was undertaken to assess clinically whether RCSP, which was appropriately combined with antegrade perfusion, could be an alternative to antegrade selective coronary perfusion in small infants undergoing the arterial switch operation.

Material and Methods

The patient population consisted of 22 infants and 11 neonates who underwent an arterial switch operation for TGA. Patients who needed ventriculotomy were excluded from the study. Depending on the type of multidose cardioplegia, the patients were randomly divided into two groups. Twenty-two patients received cardioplegic solution by RCSP, and 11 other patients received the same solution by antegrade selective coronary artery perfusion (ASCP). In the RCSP group, 17 patients had simple TGA (intact ventricular septum) and 5 patients had TGA with ventricular septal defect (VSD). Eight of them were neonates. In the ASCP group, 8 patients had simple TGA and 3 patients had TGA with VSD. The two groups were well matched with regard to preoperative profiles (Table 1). Both preoperative left ventricular pressure and left ventricular morphology (volume and muscle mass), indicative of the degree of left ventricular development, were also comparable between the groups.

Cardiopulmonary bypass was instituted by individual venous cannulation and arterial cannulation of the distal ascending aorta. The bypass flow rate was kept constant at 2.5 L/m^2/min, and the core body temperature was cooled to a rectal temperature of 28°C. The composition of the cardioplegic solution used is as follows:

Glucose, 2.5 g/L
Sodium chloride, 75 mmol/L
Sodium bicarbonate, 10 mmol/L
Potassium chloride, 20 mmol/L
Calcium gluconate, 0.6 mmol/L
Lidocain, 100 mg/L
Albumin, 10 g/L
Osmolarity, 340 mosm/L

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Table 1. Study Group Characteristics

Variable	RCSP Group (n = 22)	ASCP Group (n = 11)
Age (mo)	5.3 ± 2.8	4.4 ± 1.7
Weight (kg)	7.9 ± 13.1	4.7 ± 6.0
Neonates	8	3
TGA		
With IVS	17	7
With VSD	5	4
LVp/RVp	0.90 ± 0.08	0.92 ± 0.10
LVEDV (% normal)[a]	202 ± 70	189 ± 62
LV mass (% normal)[a]	72 ± 22	67 ± 18

[a] LVEDV and LV mass were obtained on the basis of biplane angiography and are expressed as percent of normal values.

ASCP = antegrade selective coronary perfusion; IVS = intact ventricular septum; LV mass = left ventricular muscle mass; LVEDV = left ventricular end-diastolic volume; LVp = left ventricular peak pressure; RCSP = retrograde coronary sinus perfusion; RVp = right ventricular peak pressure; TGA = transposition of the great arteries; VSD = ventricular septal defect.

The initial cardioplegic infusion (15 mL/kg) was performed by injection from the aortic root in both groups. The following infusion (7 mL/kg) was performed through one of the two techniques of delivery in each group, however, and it was repeated at 30-minute intervals until reconstruction of the ascending aorta was completed. Then, an additional infusion was administered antegradely from the "new" aortic root in both groups. Topical cooling with ice slush was also used during ischemia. Calcium ion concentration in the bypass perfusate was intentionally maintained at low levels (0.4 to 0.6 mmol/L) during ischemia and early reperfusion, and it was corrected after 15 minutes of reperfusion. All surgical procedures for correction including closure of the atrial and ventricular septal defects and reconstruction of the pulmonary artery were performed during aortic cross-clamping in all patients.

Perfusion Technique in the Retrograde Coronary Sinus Perfusion Group

After cardiac arrest was induced by the initial cardioplegic infusion, the right atrium was opened. A balloon-tipped catheter (6F Foley catheter) was advanced as far as 1 cm into the lumen of the coronary sinus and inflated with 0.5 mL of water. The catheter was then gradually pulled back until the inflated balloon was wedged to the membranous flap (sometimes to the thebesian valve) at the orifice of the coronary sinus. Gentle traction was maintained on the catheter during cardioplegic infusion to avoid occluding early branches of the coronary sinus. The cardioplegic solution was infused through the balloon catheter by the gravity of a 50-cm height. The cardioplegic effluent was observed issuing from both coronary ostia in all infusions. The duration of each perfusion was about three minutes. The balloon catheter was left in place during its use.

Perfusion Technique in the Antegrade Selective Coronary Perfusion Group

A 6F Foley catheter, the balloon tip of which had been cut off, was used for selective coronary artery perfusion with cardioplegic solution. Direct cannulation into both coronary ostia was repeatedly conducted during each infusion. The perfusion was performed by the gravity of a 100-cm height; consequently, the duration of infusion for one coronary artery was about 30 seconds.

After about 30 minutes of reperfusion, the patients were weaned from cardiopulmonary bypass while the pressures of the left atrium, central vein, and radial artery were closely monitored. On the basis of these hemodynamic variables as well as the need for catecholamine support, the postoperative hemodynamic state was assessed 30 minutes after termination of cardiopulmonary bypass. Blood samples to determine the release of creatine kinase isoenzyme MB (CK-MB) were obtained at specific intervals: 1, 3, 6, 12, 24, and 48 hours after aortic declamping. The total CK-MB during the 48-hour period was calculated by the method of Shell and colleagues [5], and the disapperance rate of the isoenzyme from blood (0.0664/h) was calculated as the average value in all the patients.

Data Analysis

All data were expressed as the mean ± the standard deviation. Statistical comparisons between the groups were made by either Student's t test or the χ^2 test, and $p < 0.05$ was considered a significant difference.

Results

Operative data including cardiopulmonary bypass and aortic cross-clamping time and the dose of cardioplegic solution used are shown in Table 2. Although there was no difference in total dose of cardioplegic solution between the two groups, the aortic cross-clamping time and cardiopulmonary bypass time in the ASCP group were significantly longer than those in the RCSP group, which suggested that the procedure of direct cannulation to the bilateral coronary ostia in the ASCP group was time-consuming.

Table 2. Operative Data

Variable	RCSP group (n = 22)	ASCP group (n = 11)	p Value
ACC time (min)	128 ± 19	143 ± 21	<0.05
Simple TGA	125 ± 16 (n = 17)	137 ± 21 (n = 7)	NS
Complex TGA	136 ± 27 (n = 5)	153 ± 18 (n = 4)	NS
CPB time (min)	173 ± 22	196 ± 28	<0.02
Total dose of CP (mL/kg)	60 ± 15	60 ± 14	NS

ACC = aortic cross-clamp; ASCP = antegrade selective coronary perfusion; CP = cardioplegic solution; CPB = cardiopulmonary bypass; NS = not significant; RCSP = retrograde coronary sinus perfusion; TGA = transposition of the great arteries.

Table 3. Hemodynamic State Immediately After Weaning From Cardiopulmonary Bypass

Group	Dosage of Dopamine (μg/kg/min)	Arterial Systolic Pressure (mm Hg)	Heart Rate (beats/min)	Mean LAP (mm Hg)	Mean CVP (mm Hg)
RCSP (n = 22)	4.2 ± 2.8	74 ± 10	147 ± 15	6.4 ± 2.6	7.1 ± 1.8
Neonate (n = 8)	5.1 ± 2.5	71 ± 9	153 ± 16	6.5 ± 2.6	7.5 ± 1.9
ASCP (n = 11)	5.4 ± 3.4	66 ± 4	157 ± 20	6.1 ± 2.6	6.1 ± 2.3

ASCP = antegrade selective coronary perfusion; CVP = central venous pressure; LAP = left atrial pressure; RCSP = retrograde coronary sinus perfusion.

Hemodynamics at Weaning From Cardiopulmonary Bypass

After aortic declamping, sinus rhythm recovered spontaneously and ST-T changes were normalized spontaneously in a few minutes in all patients. The dosage of dopamine administered at weaning from cardiopulmonary bypass was 4.2 ± 2.8 μg/kg/min in the RCSP group and 5.4 ± 3.4 μg/kg/min in the ASCP group, and no patient needed epinephrine. Eight neonates in the RCSP group could also be weaned from bypass with a similar amount of dopamine (5.1 ± 2.5 μg/kg/min). There were no significant differences in hemodynamic indexes such as arterial pressure, heart rate, left atrial pressure, and central venous pressure between the two groups. Both groups were able to achieve stable hemodynamics at a low preload (low left atrial and central venous pressure). The central venous pressure in the neonates tended to be higher than in the older patients; however, the mean value was still about 7 mm Hg, indicating that satisfactory myocardial protection was provided in the neonates as well as in the older infants (Table 3).

Creatine Kinase-MB Level After Reperfusion

The serum levels of CK-MB showed no significant differences between the two groups at any sampling time after reperfusion. Both groups reached a peak level of CK-MB immediately after aortic declamping (after 1 hour of reperfusion) and then showed a progressive decrease in its level during the ensuing period (Fig 1). The peak value of CK-MB was 105 ± 35 IU/L in the RCSP group and 119 ± 66 IU/L in the ASCP group. The mean total CK-MB in the RCSP group (107 ± 51 IU/L) was low but not statistically different from that of the ASCP group (168 ± 110 IU/L). The neonatal patients in the RCSP group also had similar values of these enzymatic indexes (Fig 2).

Postoperative Clinical Course

All patients established hemodynamic stability with or without dopamine support. The total dose and maximal dosage of dopamine required were 17.2 ± 20.2 mg/kg and 4.6 ± 4.5 μg/kg/min, respectively, in the RCSP group and 17.5 ± 32.1 mg/kg and 3.8 ± 1.0 μg/kg/min, respectively, in the ASCP group. The postoperative clinical course, which was evaluated based on the dose of required catecholamine and the duration of ventilatory support, showed no significant difference between the two groups, although the neonates tended to need a larger amount of dopamine (total dose, 34.6 ± 12.6 mg/kg; maximum dosage, 8.1 ± 4.1 μg/kg/min) than older patients (Table 4).

Comment

The method of retrograde cardioplegic perfusion has already been studied by many investigators both experimentally [10–14] and clinically [2, 15]. Menasche and associates [1] reported the ability of the technique to avoid coronary ostial trauma as well as its simple perfusion procedure in patients who are operated on through an aortotomy. This benefit led us to apply the method of RCSP to patients undergoing an arterial switch operation [3]. In small infants, especially in neonates, the coronary main trunks proximal to the first branching are too short to allow uniform cardioplegic distribution by selective perfusion through a directly cannulated catheter; moreover, they are susceptible to mechanical trauma. Idriss and associates [16] reported 1 neonatal case of postoperative coronary occlusion presumably resulting from an

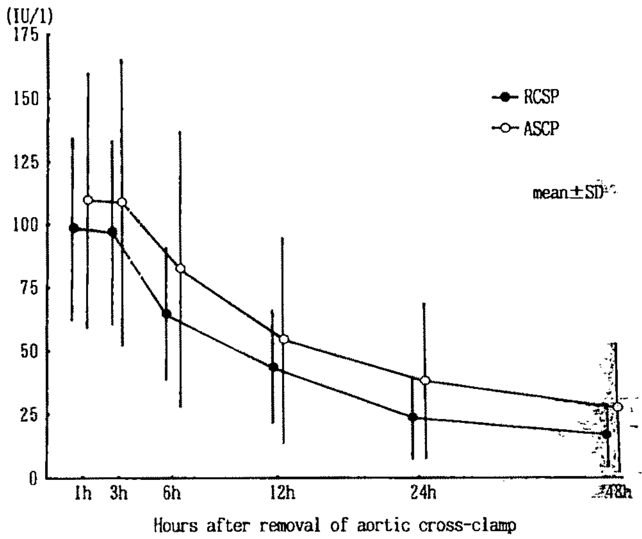

Fig 1. Serum creatine kinase-MB level after reperfusion in the retrograde coronary sinus perfusion (RCSP) group and the antegrade selective coronary perfusion (ASCP) group. There was no significant difference between the groups at any sampling time. (RCSP group, n = 22; ASCP group, n = 11.)

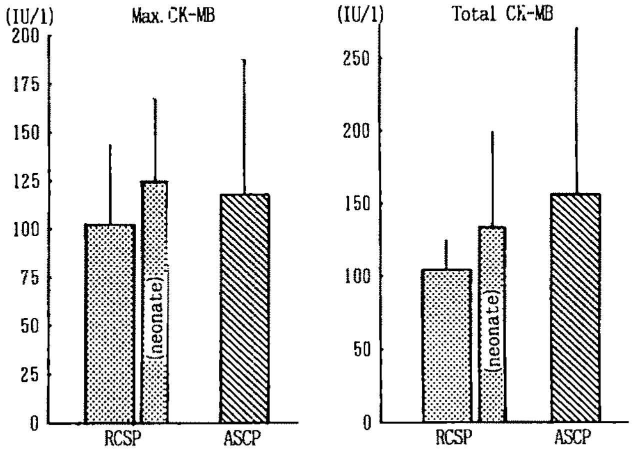

Fig 2. Maximum creatine kinase-MB (CK-MB) *and total released CK-MB in the retrograde coronary sinus perfusion* (RCSP) *group and the antegrade selective coronary perfusion* (ASCP) *group.* Wide columns *represent total patients in each group. A* narrow column *represents neonatal patients (n = 8) in the RCSP group. There were no significant differences in these enzymatic indexes between the groups and between neonates and older patients. (RCSP group, n = 22; ASCP group, n = 11.)*

injury by the cardioplegic catheter after arterial switch operation. These observations indicate that RCSP in infants undergoing arterial switch operation could presumably produce the same or even greater advantages than are presently afforded adults undergoing aortic valve operations.

In the present study, the postoperative hemodynamics, serum CK-MB level, and clinical course were comparable between the RCSP and ASCP groups. In both groups, the peak of serum CK-MB was noted in the early phase of reperfusion, and its level then progressively decreased, indicating that both methods of cardioplegic delivery provided good myocardial protection. Furthermore, the neonatal patients in the RCSP group also showed good results, similar to those of the older patients. From a technical viewpoint, RCSP also showed some excellent advantages. Because the catheter for RCSP was kept in the coronary sinus during ischemia, cardioplegic infusion could be repeated as often as necessary without any interruption in the operative procedures. Indeed, the aortic cross-clamping time of the RCSP group was shorter than that of the ASCP group.

Table 4. Postoperative Clinical Course

Group	Total Dose of Dopamine (mg/kg)	Maximum Dosage of Dopamine (μg/kg/min)	Intubation Time (days)
RCSP (n = 22)	17.2 ± 20.2	4.6 ± 4.5	2.5 ± 1.1
Neonate (n = 8)	34.6 ± 12.6	8.1 ± 4.1	3.3 ± 0.5
ASCP (n = 11)	17.5 ± 32.1	3.8 ± 1.0	3.3 ± 2.8

ASCP = antegrade selective coronary perfusion; RCSP = retrograde coronary sinus perfusion.

Recently, successful arterial switch operations for TGA have been reported at several institutions [16–19]. Most of them used either a single dose of cardioplegia [16, 17] or profound hypothermia and circulatory arrest without cardioplegia [19]. DeLeon and co-workers [20] compared single-dose and multidose cardioplegia for myocardial protective effect and concluded that the single dose was both simple and effective in infants undergoing arterial switch operations. In an effort to reduce ischemic time, they closed any existing atrial and ventricular septal defects before aortic cross-clamping and reconstructed the pulmonary artery during rewarming after release of the aortic clamp. In the present study, however, we safely performed all surgical procedures during aortic cross-clamping to accomplish precise repair in a bloodless field. Indeed, in our hospital, only four operative deaths occurred among 88 patients who underwent arterial switch operations under the same cardioplegic procedure until November 1989. There appeared to be an obvious technical difference with respect to the accuracy of reparative procedures in a beating heart and those in a cardioplegic-arrested heart. Corno and associates [21] reported that multidose cold blood cardioplegia of appropriate ion components provided the best myocardial protection in neonatal hearts. Our previous work [22] also demonstrated multidose administration of our cardioplegic solution to be effective in myocardial recovery after prolonged ischemic arrest in infants. On the basis of these findings, and considering the role of coronary collateral in clinical situations, we believe that multidose cardioplegia administered throughout the ischemic period is essential for preservation of ventricular function in prolonged ischemic arrest.

Some experimental studies [23–25] have shown that RCSP poorly perfused the right ventricular free wall and interventricular septum while it adequately perfused the left ventricular region to reach the capillary level [23, 25]. Most clinical studies, however, have shown no evidence of any impaired functional preservation of the right ventricle [1, 2]. The discrepancy between these experimental and clinical findings appears to be attributable mainly to (1) use of topical hypothermia in the latter setting and (2) the favorable venous drainage pattern of the human right ventricle [11, 24]. In the present study, there were no problems of right ventricular preservation in the RCSP group, as evidenced by the right atrial pressure and enzymatic index similar to that of the ASCP group, although these variables may lack sufficient sensitivity to establish any mild right ventricular damage. In hearts treated with retrograde cardioplegia, Shaper and co-workers [15] demonstrated the occurrence of myocardial edema and microvascular damage and suggested that continuous perfusion with noncolloid-osmotic solution might be one of the causes of these detrimental effects. We used an asanguineous but albumin-containing solution for the mode of intermittent perfusion, which may have contributed to our good results.

In conclusion, in the present clinical study we demonstrated that the combination of retrograde cardioplegia with aortic root cardioplegia could provide as good myocardial protection as ASCP even in small infants. Furthermore, RCSP was shown to be superior to selective coronary artery perfusion in regard to the technical simplicity of the perfusion procedure and is presumed to provide a greater benefit in avoiding coronary ostial trauma. Therefore, RCSP is an attractive alternative to direct coronary artery cannulation for cardioplegic delivery in infants undergoing arterial switch operation.

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Recurrent Thymoma in Patients With Myasthenia Gravis

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One hundred sixty-six patients underwent operation for myasthenia gravis between 1977 and 1989. Thirty-eight patients had associated thymoma, registering stages I (n = 17), II (n = 9), III (n = 11), and IVa (n = 1) according to the classification of Masaoka and colleagues. Extended thymectomy was performed on 128 patients without thymoma; thymothymectomy, with resection of the anterior mediastinal fat and tissues adherent to the tumor, was performed in all patients with thymoma. There were no instances of early or late death. Neuromuscular function improved, and clinical myasthenic symptoms stabilized in almost all patients except 2 patients in stage III and 1 patient in stage IVa, who had an exacerbation of the myasthenic symptoms associated with recurrence of thymoma. All the recurrent tumors were on the pleura and could be resected. The suspected cause of recurrence is either dissemination of tumor cells as a result of operative manipulation or undetected disseminated foci that existed at the time of the first operation. The resections of the recurrent invasive thymomas localized on the pleura were easily performed and improved the myasthenic symptoms.

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Thymomas have been reported in 9% to 28% of patients with myasthenia gravis (MG) [1–3]. Thymothymectomy can improve myasthenic symptoms, but MG is liable to recur in association with recurrence of the thymoma [4–6]. Thymoma cannot be classified as benign or malignant on the basis of histological findings alone, and prognosis appears to be more closely related to gross characteristics at the time of the operation than to histological findings. Metastatic thymoma frequently involves the pleura or the diaphragm, whereas extrathoracic metastases are uncommon [7, 8].

We describe the clinical patterns of MG with thymoma and present 3 cases of recurrence on the pleura. The efficacy of a second resection of recurrent thymoma localized on the pleura is also discussed.

Material and Methods

From June 1977 to May 1989, we had 166 patients with MG in the Division of Thoracic and Cardiovascular Surgery at Sendai National Hospital. Age distribution of the patients is shown in Figure 1. The average age was 38 years (range, 3 to 77 years), and the peak period of MG recurrence was in the third decade. Fifty-eight patients were male and 108 patients were female. Among 166 patients with MG, 38 had thymomas. The average age of patients with thymoma was 46 years (range, 25 to 74 years). Thymoma was present in 29.3% (17/58) of male patients and 19.4% (21/108) of female patients.

Thirty-one patients had ocular MG, 10 had bulbar MG, and 125 had generalized MG. All patients with thymoma had generalized MG except for 2: 1 with ocular and 1 with bulbar MG.

The clinical stage of the patients with thymoma, according to the classification of Masaoka and colleagues [9], was defined as follows: stage I (17 patients), macroscopically encapsulated and with no microscopic capsular invasion; stage II (9 patients), either macroscopic invasion into surrounding fatty tissue or mediastinal pleura, or microscopic invasion into capsule; stage III (11 patients), macroscopic invasion into neighboring organ, ie, pericardium, great vessels, or lung; stage IVa (1 patient), pleural or pericardial dissemination; and stage IVb (none), lymphogenous or hematogenous metastasis.

Operations were performed through a median sternotomy. An extended thymectomy [10] was performed in 128 patients without thymoma. An extended thymectomy, including thymoma, was performed in 17 patients in stage I and 9 patients in stage II. The mediastinal pleura, adherent to the thymoma, was resected in all patients in stage II. All patients in stages III and IVa underwent extended thymectomy and resection of the thymoma. Additional surgical procedures performed were resection of mediastinal pleura (12 patients), pericardium (6 patients), lung (5 patients), phrenic nerve (3 patients), superior vena cava (1 patient), left innominate vein (1 patient), and pleural implant (1 patient).

Six patients in stage III and 1 patient in stage IVa received postoperative radiation therapy to the mediastinum at doses between 16.5 and 50 Gy. Almost all patients were treated with small doses of anticholinergic drugs, alternate-day corticosteroids, or both.

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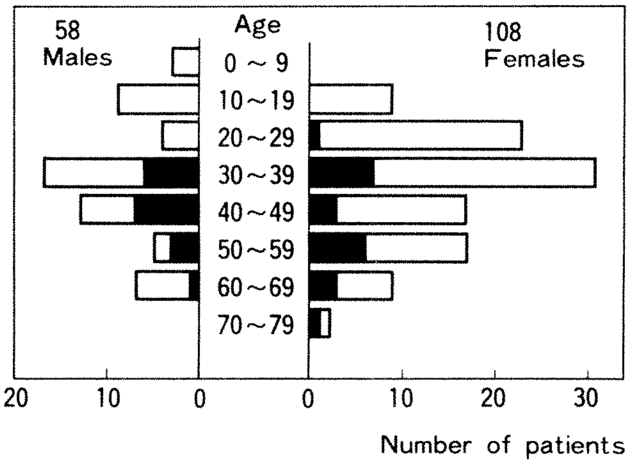

Fig 1. Age distribution of patients. Open bars *indicate patients without thymoma;* closed bars *indicate patients with thymoma.*

Results

There were no instances of early or late death after operation during the follow-up period. Although the patients required various times for myasthenic symptoms to improve, the doses of anticholinergic drugs and corticosteroids could be tapered while neuromuscular function increased and clinical MG stabilized in almost all patients. No patient in stages I or II showed recurrence of thymoma. Among the patients in stages III and IVa, 3 patients with recurrent thymoma on the pleura had an exacerbation of myasthenic symptoms. After resection of the recurrent thymomas, the myasthenic symptoms improved greatly.

Case Reports

Patient 1

A 40-year-old man was admitted to our hospital in June 1977 with a 3-month history of diplopia and ptosis of the left eyelid. Chest roentgenograms showed a right upper anterior mediastinal mass. At operation, a thymic tumor invading the mediastinal pleura, the upper lobe of the right lung, and the left innominate vein was found. The tumor, including the thymus and the mediastinal fat, was resected, as was the upper lobe of the right lung adherent to the tumor. Pathology of the tumor showed a 6 × 6 × 2-cm, firm, gray-white, poorly encapsulated nodular mass weighing 45 g and a predominantly epithelial type of invasive thymoma with some lymphocyte infiltration. The postoperative course was uneventful, and ptosis was not proven at the time of discharge.

Four years after operation, the patient was receiving ambenonium chloride (15 mg/day), but diplopia and ptosis of the left eyelid reappeared. Chest roentgenograms showed two round shadows on the right diaphragm. There were no signs of local recurrence at the upper anterior mediastinum (Fig 2A). Computed tomography detected several round masses on the right diaphragm and at the right lateral margin of the pericardium (Fig 2B).

The second operation was performed on July 17, 1981, through a right posterolateral thoracotomy. There was no pleural effusion or recurrent tumor at the upper anterior mediastinum. There were four walnut-sized pieces of tumor: three on the diaphragm and one on the visceral pleura of the lower lobe of the right lung. Furthermore, there were five small tumors, a few millimeters in diameter, on the parietal pleura of the posterolateral chest wall. Adhesion of the tumors to the diaphragm and the lung were loose, so that the tumors were easily resected. The histological pattern was a predominantly epithelial type with an increased epithelial element as compared with the tumor resected in the first operation (Fig 3). The patient has been doing well on ambenonium chloride (20 mg/day) and prednisolone (15 mg) on alternate days.

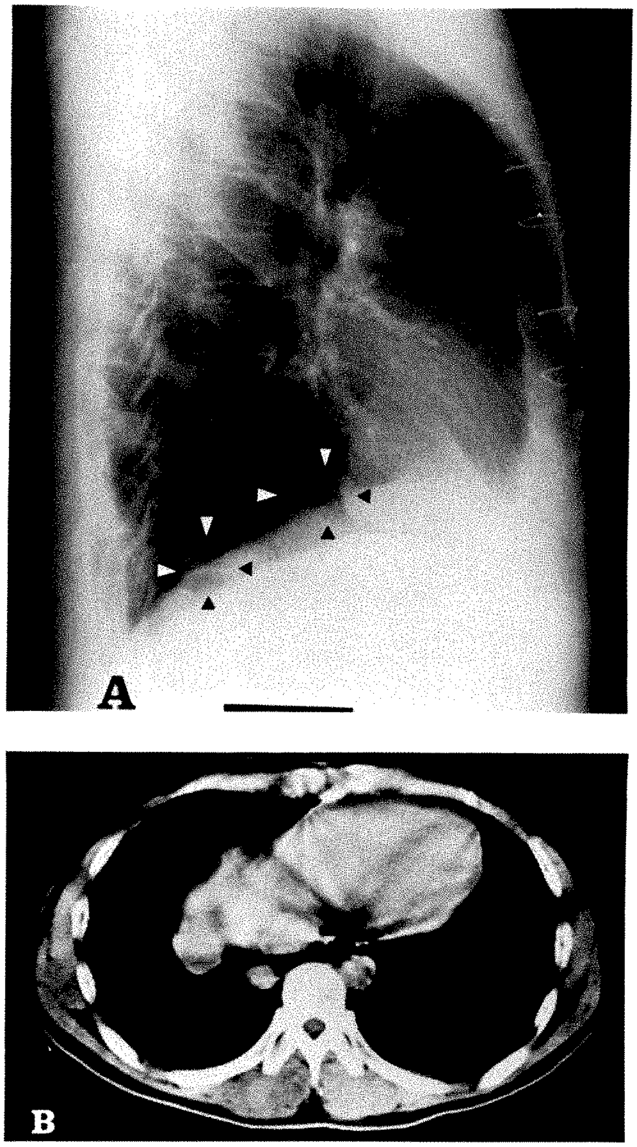

Fig 2. (Patient 1.) (A) Lateral chest roentgenogram taken before second operation. Two round shadows on the diaphragm are indicated by arrowheads. *(B) Computed tomography shows several mass shadows at the right lateral margin of the pericardium.*

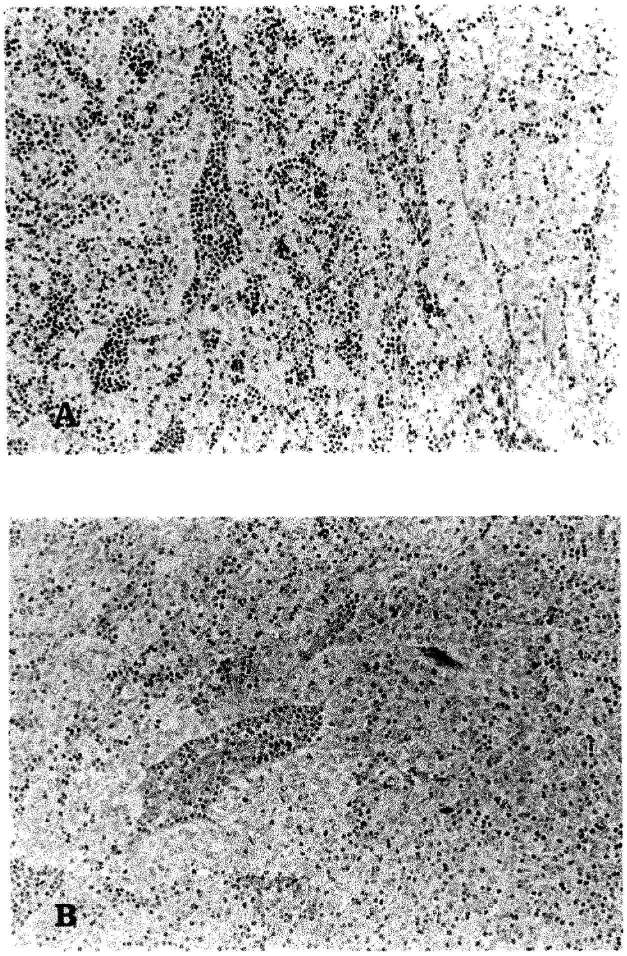

Fig 3. (Patient 1) (A) Microscopic section of thymoma resected in the first operation shows a predominantly epithelial type (hematoxylin and eosin, ×500 before 52% reduction). (B) Microscopic section of recurrent thymoma resected in the second operation shows a predominantly epithelial type with an increased epithelial element as compared with the tumor resected in the first operation (hematoxylin and eosin, ×500 before 52% reduction).

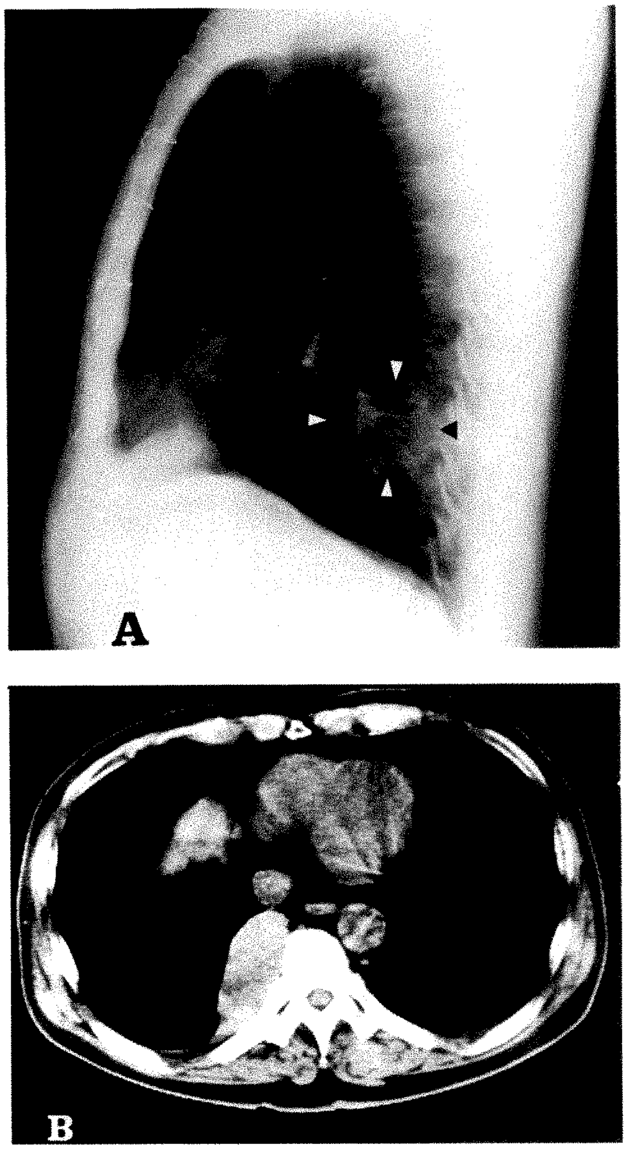

Fig 4. (Patient 2.) (A) Lateral chest roentgenogram taken before second operation shows a mass shadow, 5 cm in diameter, at the lower posterior pleural cavity (arrowheads). *(B) Computed tomographic scan shows tumors on the right posteromedial parietal pleura and at the right lateral margin of the pericardium.*

Patient 2

A 48-year-old man was admitted with complaints of weakness of the extremities, dysphagia, and ptosis of the eyelids. Chest roentgenograms showed a right anterior mediastinal mass. A diagnosis of MG with thymoma was made, and the patient underwent operation on November 7, 1980, which showed a tumor invading the pericardium and the upper lobe of the right lung. The tumor, including the thymus and the anterior mediastinal fat, was resected, as was the upper lobe of the right lung and the pericardium adherent to the tumor. Pathological study of the tumor showed it to be a 10 × 9 × 3-cm, solid, encapsulated thymoma weighing 131 g. Dense adhesions were present between the capsule of the tumor and the lung and pericardium. There was a capsular invasion of the tumor, and the histological pattern was predominantly epithelial thymoma. The postoperative course was stormy. Respiratory support was needed for 5 days during the early postoperative period. Postoperative radiation therapy was discontinued at a dose of 16.5 Gy because the patient had severe general fatigue, and neuromuscular function did not improve greatly. The patient received two sessions of pulse therapy with 1,000 mg of methylprednisolone for 3 days in December 1986 and plasma exchanges in September 1987, while the symptoms of MG became exacerbated. The patient was receiving ambenonium chloride (30 mg/day) and prednisolone (35 mg) on alternate days.

In April 1988 a mass shadow, 5 cm in diameter, at the right lower posterior pleural cavity was noticed on a routine follow-up chest roentgenogram (Fig 4A). Computed tomography detected an abnormal mass adherent to the parietal pleura at the right posteromedial pleural cavity and two abnormal masses at the lateral margin of the pericardium (Fig 4B). A diagnosis of a recurrent thymoma was made, and a second operation was performed on June 17, 1988, through a right posterolateral thoracotomy. There were three separate tumors. The largest tumor was an 8 × 4 × 3-cm, nodular mass weighing 55 g that invaded the parietal pleura of the posterobasal chest wall. The other two small tumors invaded the diaphragm and the posterobasal segment of the lower lobe of the right lung. All tumors were resected. The histological pattern of the tumors was predominantly epithelial thymoma. The symptoms of MG improved dramatically soon after the second operation. The patient has been doing well on ambenonium chloride (20 mg/day) and prednisolone (15 mg) on alternate days.

Patient 3

A 33-year-old woman was admitted to our hospital with a 1-month history of ptosis of the right eyelid and dysphagia. Myasthenia gravis was diagnosed as the result of a positive Tensilon test. At the time of her admission, a chest roentgenogram showed a mass at the left anterior mediastinum. An operation was performed on March 14, 1983, through a median sternotomy. The 5 × 3 × 2-cm tumor, originating from the left lobe of the thymus and adhering to the sternum, was resected, and the upper lobe of the left lung and the left innominate vein were partially resected. Furthermore, a bean-sized tumor on the visceral pleura of the lower lobe of the left lung and several miliary tumors on the parietal pleura were resected. The histological pattern of the tumors was identical and proved to be thymoma of a mixed type. Postoperative radiation therapy was performed at a dose of 40 Gy. Neuromuscular function improved dramatically, and the patient was followed up.

An abnormal 3 × 4-cm mass shadow on the left diaphragm was detected on a chest roentgenogram (Fig 5A) and a computed tomographic scan (Fig 5B) in February 1988; it was associated with an increase in general weakness. The patient was receiving ambenonium chloride (30 mg/day) and prednisolone (40 mg) on alternate days. A second operation was performed on February 26, 1988, under the diagnosis of recurrent thymoma. During a left posterolateral thoracotomy, there was a 3.5 × 3 × 3-cm tumor invading the diaphragm and the posterobasal segment of the left lower lobe, where several disseminated tumors were observed. Other small tumors were located on the parietal pleura of the posterior chest wall. The largest tumor was resected, including a part of the diaphragm and a lung segment, and the other small tumors were resected. The histological patterns of these tumors were basically identical, but the epithelial element of the tumor increased as compared with the tumor resected in the first operation. Microscopic findings showed the tumor to be infiltrating the diaphragm. The postoperative course was uneventful, and the patient has been doing well on ambenonium chloride (20 mg/day) and prednisolone (20 mg) on alternate days.

Comment

The natural history of thymomas includes a variety of clinical courses. Prognosis of the tumors appears to be more closely related to the gross characteristics found at the time of operation than the histological appearance, because the histological definition of the malignant potential of these tumors is unreliable. The incidence rate of thymoma among all myasthenic patients varies from 9% to 28% [1–3], and 25% to 59% of patients with thymoma appear to have MG [1, 5, 9, 11, 12].

In our study, the incidence rate of thymoma among myasthenic patients was 22.9% (38/166). The rate of noninvasive thymoma was 44.7% (17/38), which was approximately the same as the results found by Masaoka and colleagues [9]. The 5-year survival rates are approximately 80% if the thymomas are noninvasive [12, 13] and between 23% and 42% if the thymomas are invasive [1, 12].

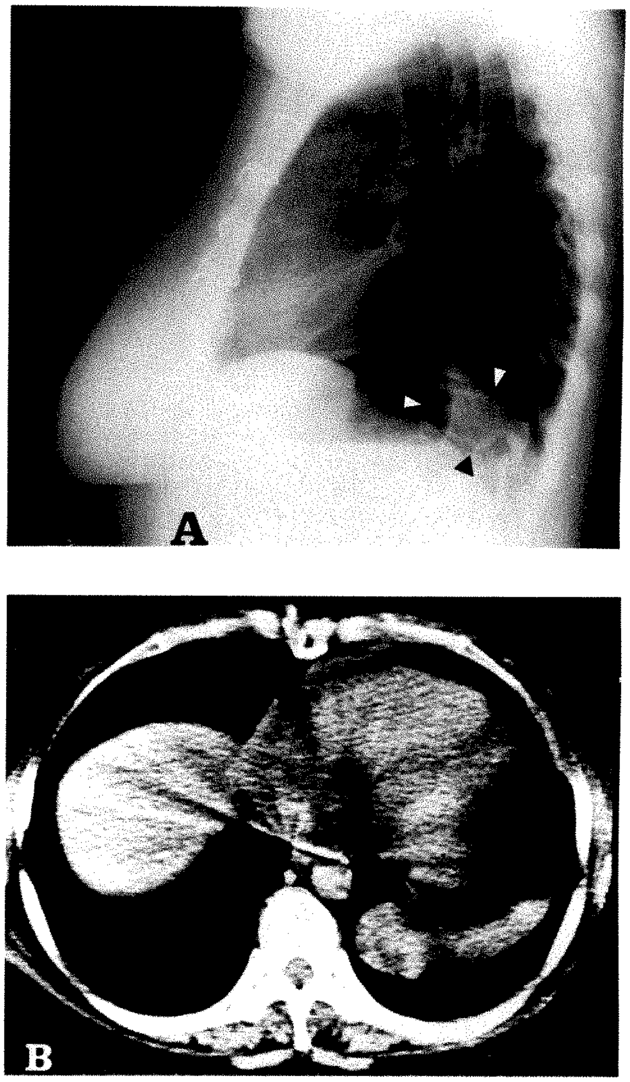

Fig 5. (Patient 3.) (A) Lateral chest roentgenogram taken before second operation shows an abnormal mass shadow on the diaphragm (arrowheads). (B) Computed tomography shows a round mass adherent to the diaphragm.

Several reports have described extrathoracic metastases and recurrence of noninvasive thymoma. Fechner [4] reported that thymoma recurred in less than 2% of patients with noninvasive thymoma who underwent operation and described two broad categories with regard to the type of recurrence in noninvasive thymoma. One category was mediastinal recurrence localized in the mediastinum without additional sites of involvement; the other was seeding or metastasis without local mediastinal recurrence. Fechner [4] did not have an explanation for these different types of recurrence but suggested that reexploration might be warranted if a patient had had a noninvasive thymoma removed and had evidence of a localized mediastinal tumor without pleural spreading. Invasive thymoma is usually a slow-growing tumor and tends to infiltrate adjacent thoracic organs by direct extension. The reason for thoracic limitation is unknown, because discontinuous metastases to the pleura are common and histological features of the metastatic tumors cannot be defined as malignant, in contrast to metastasis from carcinoma. Surgery and radiation therapy are the major therapeutic treatment methods for invasive thymoma, and an aggressive surgical approach should be attempted, even for invasive thymomas. Cohen and colleagues [14] suggested that complete resection was the most important factor affecting long-term survival. When they achieved complete resection of the tumor, they could not show a significant difference in survival rates between patients who received postoperative radiation therapy and those who did not.

The MG associated with thymoma, whether noninvasive or invasive, is more severe and brittle, and anticholinesterase control of symptoms is generally unsatisfactory. Corticosteroids are often used in patients with thymomas for the associated symptoms of MG rather than as a form of treatment for the tumor. The "thymolytic" effect of corticosteroids, especially for cortical lymphocytes, is well known. Several reports have described thymoma regression after use of corticosteroids [15–17]. After using corticosteroids to treat 6 patients with intractable MG and malignant thymoma, Haussen and colleagues [18] suggested that they might be effective in treatment of thymoma. Our 3 patients with recurrent thymoma received alternate-day corticosteroid therapy during their follow-up periods, and all the recurrent tumors showed a similar pattern of recurrence localized on the pleura. These results suggest that the alternate-day corticosteroid therapy for MG might affect the growth and metastasis patterns of recurrent thymoma.

Fewer patients with MG died of thymoma than did patients without MG, because many thymomas associated with MG are not invasive. Genkins and associates [2] recommended early thymectomy before MG progressed and suggested that a long-standing thymoma might undergo malignant degeneration on the basis of the association between malignant characteristics and delayed operation. We have adopted early thymectomy for the surgical treatment of MG so that the clinical stages of many patients with thymoma could remain in stages I and II, and so that the thymomas could be completely resected easily. Three of 12 patients in stages III and IVa had recurrence of the thymoma localized on the pleura with an exacerbation of myasthenic symptoms. The suspected causes of recurrence are either dissemination of tumor cells resulting from operative manipulation in patients 1 and 2 or undetected disseminated foci that existed at the time of the first operation in patient 3. Therefore, the potential risk of pleural implantation of malignant cells should be taken into consideration during operation to avoid spread resulting from handling of the tumor.

In conclusion, we recommend performing aggressive surgical intervention for recurrent thymoma on the pleura in MG, because resection of the tumors not only was easy to perform but also was extremely effective in improving myasthenic symptoms in our patients.

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Risks of Blood Exposure to the Cardiac Surgical Team

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The risk of transmission of human immunodeficiency virus from patient to cardiac surgical team is perceived by most people to be very slight, yet the possibility is a valid concern. The feasibility of "barrier protection" in prevention of this risk is dependent on integrity of surgical gloves and absence of splashes of body fluids into eyes and broken skin. These factors were observed and recorded in 50 coronary bypass operations and 17 valve replacements. There was a high risk of glove penetrations (one to two per team member per operation) and of skin punctures, lacerations, or eye splashes (from 0.4 to 1.5 instances per operation). Better gloves and more self-defensive surgical techniques are indicated.

(Ann Thorac Surg 1990;50:248–50)

The risk of human immunodeficiency virus (HIV) transmission from patient to health care worker is usually considered to be very slight [1–4]. Although hepatitis B is far more common and apparently much more infectious than HIV, it is usually not fatal and both natural and vaccine-induced immunity are available. Thus, acquired immunodeficiency syndrome (AIDS) is of much more concern to surgeons [5].

Articles in the medical literature and newspapers and verbal quotes on the incidence of contamination of the surgical team are retrospective and anecdotal and subject to great error. The perception of the risks involved is certainly greater in surgeons than in nonsurgeons. There has been a recent marked increase in the number of patients who have intravenous-drug–related endocarditis and require surgical replacement of a cardiac valve. In New York City, 54% of a group of intravenous-drug–addicted patients were HIV positive [6]. There has also been a steady increase in the number of repeat ("redo") coronary bypass operations; many of these patients received transfusions at their previous operation before the availability of HIV testing. Both these groups of patients represent a risk of harboring the HIV virus. Open heart operations are associated with potential exposure to large amounts of blood and an increased probability of injury to surgical team members, especially when performed under emergency or difficult conditions. Estimates of the number of needle sticks, cuts, and other exposures of surgical team members to bloodborne viruses have varied from near zero to numerous injuries each year [7, 8]. Presently available gloves are also perceived to be more fragile than they formerly were [9]. "Universal barrier precautions," so glibly recommended, are useless when a contaminated needle penetrates the skin. These concerns led us to do a prospective, objective study of the usage of gloves (reflecting their puncture or tears) and potential exposure to tissue fluids of surgical team members during coronary artery bypass grafting and valve replacement operations.

Material and Methods

Cases of open heart operation for coronary artery bypass grafts (50 operations) and single valve replacements (17 operations) from February through August 1989 were studied. Two different hospitals and nursing teams were used, but the surgical team (faculty and residents) rotated between these institutions.

A data form was completed by the circulating nurse during each operation. For each person participating in the procedure, data on (1) glove usage; (2) eye or face splashes of blood or fluids; and (3) needle, wire, or bone penetration of skin were documented. For skin injuries, it was noted whether the penetrating instrument was sterile or contaminated with the patient's blood or tissue fluids. "Exposure" was defined as puncture wounds or scratches of the skin or blood in the eyes or on glasses and adjacent face.

The time of operation from "skin incision to bandage" was noted. The presence of broken skin, rashes, or other cutaneous lesions on the hands of each team member was elicited.

Individuals observed included the surgeon; the first, second, and third assistant surgeon; the scrub nurse and second scrub nurse, the anesthesiologist; the second anesthetist (or resident); the first and second circulating nurse; the first and second perfusionist; and miscellaneous persons. In all cases, the first assistant and surgeon were an experienced faculty surgeon and a cardiothoracic resident surgeon with 6 to 8 postgraduate years of surgical training.

It is hospital policy for perfusionists and circulating nurses to wear gloves. There is no fixed policy with regard to anesthesiologists and anesthetists, and in many instances they did not use gloves. Because this study was performed only to determine the magnitude of the problem in a specific group of physicians and nurses and is of limited scope, the data were not analyzed statistically.

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Table 1. Glove Usage as a Function of Length of Operation

	Time (min)				
No. of Gloves	180–249	250–309	310–369	370–429	>430
Range	17–43	20–57	18–37	26–45	39–60
Mean	26	35	28	36	49

Results

Data regarding preexisting skin rashes or breaks in the skin of the operating team were not complete enough to allow analysis. Most members of the teams were reluctant to report minor skin lesions. The time from skin incision to bandage varied from 180 to 625 minutes (mean, 294 minutes) for coronary bypass operations and from 240 to 365 minutes (mean, 301 minutes) for valve procedures.

From 8 to 13 people were involved in each operation, a mean of 9.6 in the coronary procedures and 9.1 in the valve replacements. Every operation involved at least two surgeons, a scrub nurse, a circulating nurse, a perfusionist, and an anesthesiologist. Additional surgeons, nurses, anesthesiologists, anesthetists, and perfusionists accounted for the remainder of the personnel.

The number of gloves (two in the original pair plus each replacement) used in each operation varied from 17 to 60, with a mean of 30 (hospital 1) and 38 (hospital 2) for each coronary operation and 25 (hospital 1) and 34 (hospital 2) for valve replacement procedure. Sixty gloves were used on one repeat coronary bypass operation involving 10 people; 57 were used on a difficult redo mitral valve replacement involving 11 people. More than 90% of glove replacements were the result of loss of glove integrity rather than contamination. In very few cases, a needle, wire, or other sharp agent penetrated the glove and underlying skin. In more than 90% of instances, the gloves were either torn by a blunt instrument or simply "disintegrated" as the hand was forcibly used, as in forcing a wire through the sternum. There appeared to be little correlation between time involved in the procedure and number of gloves used (Table 1). All procedures in which fewer than 22 gloves were used were uncomplicated coronary artery bypass grafts, usually with operating times of less than 301 minutes.

Table 2. Mean Number of Gloves Used by Key Team Members in Each Operation

	CABG (n = 50)		Valve Replacement (n = 17)	
Position on Team	Hospital 1	Hospital 2	Hospital 1	Hospital 2
Surgeon	3.6	3.9	4.3	4.3
First assistant	3.3	3.5	4.3	3.6
Scrub nurse 1	4.0	3.5	3.7	3.0
Scrub nurse 2	3.6	3.0	2.5	3.0
Perfusionist 1	6.1	4.1	4.5	3.7
Perfusionist 2	3.6	4.2	2.5	4.5
Means[a]				
Per operation	30.1	38.3	34.3	25.4
Per person	4.0	3.1	3.1	2.9

[a] Circulating nurses, anesthesiologists and anesthetists either did not consistently use gloves or changed gloves when moving from room to room rather than just when they were punctured; therefore, data on their usage is not shown in except in "Mean."

CABG = coronary artery bypass graft.

Table 3. Exposures (Incidences per 100 Cases)

	CABG (n = 50)		Valve Replacement (n = 17)	
Position	n	%	n	%
Puncture with contaminated needle, wire, or bone				
Surgeon	1	2	7	41
First Assistant	3	6	7	41
Nurse	6	12	4	24
Total	10	20	18	106
Puncture with sterile agent				
Surgeon	1	2	. . .	. . .
First Assistant	2	4	2	12
Nurse	4	8	1	6
Total	7	14	3	18
Cut with used scalpel				
Circulating nurse	. . .	. . .	1	6
Total	0	0	1	6
Electrocautery burn through glove				
Surgeon	1	2	. . .	. . .
First Assistant	1	2	. . .	. . .
Total	2	4	0	0
Blood in eyes and/or glasses				
Surgeon	1	2	2	12
First Assistant	. . .	. . .	1	6
Total	1	2	3	18
Total exposures	20	40	25	147

CABG = coronary artery bypass graft.

Except for perfusionists in hospital 1, there was little difference in glove usage by various members of the team (Table 2). In this hospital, it is a policy that gloves be changed by the perfusionist as soon as blood contaminates the glove, not when it is perforated.

Exposures and types of injuries are shown in Table 3. The surgeon, first assistant, and scrub nurses were the only people (other than one circulating nurse who had a scalpel cut) who sustained injuries.

Comment

Although we have no objective comparative data on previous experience or on other types of operations, this study clearly indicates the frequent failings of "barrier protection" of surgical gloves.

A study in 1980 [10] showed that about 12% of gloves used in the operating room for various types of operation were punctured. In the present study, 8 to 13 people were involved in each operation; they initially used 16 to 26 gloves. These gloves were replaced (usually for penetration or tearing) in one to 32 instances. Our "penetration rates" ranged from 5% to 81% of gloves used in each operation.

Exposures could be expressed as: (1) per operation, (2) per 100 operations, or (3) per 1,000 hours of operating time. Because the length of operating time was not well correlated with glove usage or exposures, we preferred to use the number of exposures per 100 operations (roughly a year's experience for many thoracic surgeons). Total exposures do not include the many more cases of glove punctures or tears that occurred on hands with scratches, abrasions, or rashes; therefore, these exposures represent a significant underestimation of the true risk of blood exposure. Although coronary graft operations were associated with a risk of exposure to a single member of the operating team of only 0.4 exposures per case, the cumulative risk in 100 operations is considerable.

A recent, retrospective study of about 200 surgeons showed puncture injuries recalled by 86% during the preceding year (mean, two punctures per year) [8]. Expressed as frequency per 1,000 hours in the operating room, distributions were as high as 42 to 250 injuries per 1,000 operating room hours. The data in our present study, when calculated similarly, yielded means of 16 exposures per 1,000 hours during coronary bypass procedures and 106 exposures during 1,000 hours of valve replacement procedures. Thus, our observations are comparable with those of the recent study [8], which apparently involved all types of operations; open heart operations, as we report, obviously involve far more exposure to blood and more intense surgical manipulations than most other procedures. Use of heavy wires and needles, presence of bone splinters, and considerable hardware increase the likelihood of injury. An individual scrub nurse may participate in 300 or more open heart operations per year; such an experience could expose the nurse 60 times per year.

Because exposures were based on actual breaks of skin integrity or splashes of blood in the eyes and not on the hundreds of torn gloves and saturated gowns, our estimates of risks are certainly low. The incidence of HIV-positivity remains fairly low; however, in drug addicts in some localities, it is more than 50% [6]. Converting exposure to blood and body fluids to a risk of inoculation with virus or establishment of infection is impossible with available facts. A single needle stick with HIV-positive blood may produce a risk of infection of 0.4% to 1.6% [1].

The often quoted advice to "follow the universal precautions of the Centers for Disease Control" has intuitively been recognized by surgeons as futile during critical operations; the present data illustrate the absurdity of expecting these guidelines to be of significant value in protecting the surgical team.

Many surgeons, including me, frequently use the fingers to handle tissues (such as heart or lung) because they are less traumatic than retractors or instruments. Such a technique, when needles or wires are being used (eg, valve replacements, sternal closures) pose the danger of glove or even skin damage. Surgical technique, especially that taught to resident surgeons, should be modified in view of the epidemic of bloodborne viral infections associated with the drug addiction epidemic and more nonrepressed sexual practices.

This study leads to several conclusions.

1. Open heart operations carry a high risk of skin punctures and splashes to the operating team. This risk may be of significance when dealing with HIV-positive or hepatitis B-positive patients.
2. The quality of surgical gloves should be improved.
3. Surgeons and nurses should remain constantly on guard from skin or mucous membrane contamination and injury. Better techniques, designed to lower risks to the nurses and surgeons, should be developed, taught, and practiced.

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Modification of Supraventricular Tachyarrhythmias by Stimulating Atrial Neurons

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The effects of stimulating the right atrial ventral ganglionated plexus on ventricular performance during atrial tachycardia was studied in 8 lightly sedated (pentobarbital, 2.5 mg/kg intravenously) dogs with sterile pericarditis. Atrial arrhythmias were induced by electrical stimulation (10 V, 4 ms, 100 Hz) of the right atrium through previously inserted temporary bipolar pacemaker wires. Various types of supraventricular tachycardias were produced. Atrial fibrillation was produced in 3 dogs, atrial tachycardia in all 8 dogs, different atrioventricular nodal ectopic rhythms in 6 dogs, and atrial flutter in 1 dog. These arrhythmias were associated with irregular ventricular contractions that resulted in low ventricular pressures during many cardiac cycles such that low or no aortic pressure was generated. Right atrial ventral ganglionated plexus stimulation induced slowing of ventricular rate so that every ventricular contraction resulted in aortic pressure generation, thus increasing mean aortic pressure. Responses elicited by atrial ganglionated plexus stimulation were eliminated after atropine administration. We conclude that electrical stimulation of the right atrial ventral ganglionated plexus results in slowing of ventricular contractile rate during supraventricular tachycardia, presumably by activating efferent vagal neuronal elements, thereby improving ventricular performance. If applicable in humans, this technique may be of use in management of postoperative atrial arrhythmias after cardiac operations.

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Postoperative supraventricular arrhythmias are a complication of cardiac operations. The incidence of such arrhythmias has been reported to range from 20% to 100%, depending on the method of monitoring postoperative recovery [1]. In 10% to 20% of reported cases of supraventricular arrhythmias, left ventricular performance was affected in a way that decreased left ventricular efficiency [2]. Impairment of left ventricular function was due primarily to shortened filling times, resulting in low cardiac output. In these instances, control of ventricular rate has been the goal of therapy to improve left ventricular performance. Pharmacological interventions have been used, interventions that are either short-lived or require a long time to initiate an effect. Cardioversion in the postoperative patient has also been used, a method that requires anesthesia and intubation.

Ganglia and nerves are located in the region of the interatrial groove on the ventral surface of the canine right atrium imbedded in fat. Neurons in the right atrial ventral ganglionated plexus have been identified by vital staining and histological techniques [3]. Neurons in this ganglionated plexus exert predominantly parasympathetic effects on the heart when stimulated [4], which is in keeping with the assumption that they contain primarily efferent postganglionic parasympathetic neurons [5, 6]. However, efferent sympathetic neural elements, including postganglionic sympathetic somata, have been proposed to exist in atrial and ventricular ganglionated plexi as well [3, 7, 8]. In addition, varied cardiac responses can be elicited by stimulating the neural elements in atrial ganglionated plexi in anesthetized animals. Whether parasympathetic or sympathetic effects predominate when this ganglionated plexus is stimulated in lightly sedated animals is not known. Neither is it known whether such stimulations can modify the effects of supraventricular arrhythmias on left ventricular dynamics. Therefore, in the present study, the effects of electrical stimulation of the right atrial ventral ganglionated plexus on ventricular rate during supraventricular arrhythmias were studied in lightly sedated animals to determine whether left ventricular pressure could be altered thereby and, if so, in what fashion.

Material and Methods

Animal Preparation

Experiments were performed on 8 mongrel dogs weighing 19 to 38 kg, in accordance with guidelines for animal experimentation described in "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985) and "Care of Experimental Animals — A Guide for Canada." An intravenous drip of normal saline solution was begun. Thereafter, animals were anesthetized with sodium pentobarbital (an initial dose of 300 to 350 mg intravenously, followed by a constant infusion of doses appropriate to maintain a surgical plane of anesthesia) and supported with a positive-pressure respirator. Sodium thiopental (12 to 15 mg/kg) was administered intravenously at least every hour throughout the operation or more frequently as required to maintain anesthesia. A right-sided thoracotomy was performed at the fifth

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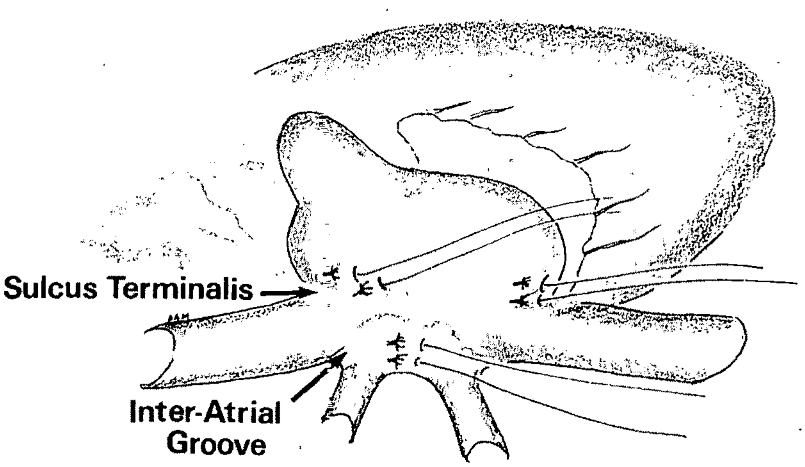

Fig 1. Ventral surface of the right atrium showing sites where the three bipolar electrodes were located. The two bipolar electrodes in atrial tissue adjacent to the cranial aspect of the sulcus terminalis and the inferior vena cava were subsequently used to induce supraventricular tachydysrhythmias. The third pair of electrodes in the fat pad on the ventral surface of the middle of the right atrium adjacent to the right pulmonary vessels was used to stimulate the right atrial ventral ganglionated plexus.

intercostal interspace, and the pericardium was opened to expose the heart.

Three pairs of temporary pacemaker wire electrodes (Weck No. 277935 electrodes coated with FEP polymer except for the tip) were sutured on selected right atrial sites. Bipolar pacing electrodes were placed for subsequent induction of supraventricular tachydysrhythmias adjacent to the cranial aspect of the sulcus terminalis and at the inferior vena caval–left atrial junction (Fig 1). Another pair of sterile bipolar electrodes was sutured into the middle of the right atrial ventral fat pad where the right atrial ganglionated plexus is located [3]; this structure lies on the ventral surface of the right atrium medial to the pericardial reflection (Fig 1). The electrodes consisted of wires insulated to within 2 mm of their tips. They were brought out through the chest wall and placed in a subcutaneous pouch in the dorsum of the neck. Then the atrial and ventricular surfaces were dusted with sterile talcum powder. A sterile gauze was placed on the right and left atrial free walls to induce, with the talcum powder, sterile pericarditis as described by Pagé and colleagues [9]. The pericardium was closed with interrupted sutures. The chest was closed in layers, residual air was withdrawn, and the animals were allowed to recover. Antibiotics were administered postoperatively, and analgesic therapy was administered as needed.

Ganglionated Plexus Stimulations

The second stage of the experiment was performed on the seventh to the fourteenth postoperative day. Sodium pentobarbital (2.5 mg/kg) was administered intravenously to the animals for light sedation, with repeated doses as required throughout the experiment. Cannulas attached to model 80 Trantec Bentley transducers were placed into the femoral arteries and led to the left ventricular cavity and the intrathoracic aorta. Aortic and left interventricular chamber pressures were recorded on a Beckman type 504 dynograph eight-channel pen recorder along with a lead II electrocardiogram. The pacemaker wires were identified under the skin and exposed through a small skin incision.

Electrical pacing of the right atrium was performed to induce supraventricular tachydysrhythmias. In the first 3 animals, this was done on the second, third, fourth, and seventh postoperative days. As no sustained arrhythmias were induced on the second, third, and fourth postoperative days, stimulations were performed in these and all other animals on the seventh to fourteenth postoperative days. This was accomplished by stimulating one pair of the atrial bipolar electrodes with a Grass SD9 square-wave stimulator, the output of which was monitored on a Tektronix D13 dual-beam oscilloscope. Various stimulating variables were used. We found that 10-V, 4-ms, and 100-Hz trains of stimuli lasting for 30 seconds to 1 minute were best for consistently inducing sustained atrial arrhythmias. Lesser voltages or frequencies did not induce sustained arrhythmias. By these means, arrhythmias lasting more than 4 minutes after termination of the stimulation were generated and therefore were classified as sustained arrhythmias.

When cardiac rhythm was normal, the bipolar electrodes placed in the right atrial ventral ganglionated plexus were activated by 15-V, 5-ms, 20-Hz stimuli, which were monitored on an oscilloscope. Then sustained arrhythmias were reinduced and, after 1 minute of sustained arrhythmia, the right atrial ventral ganglionated plexus was restimulated as described above. Thereafter, atropine sulfate (1 mg/kg) was administered intravenously and, after induction of the arrhythmia, the right atrial ventral ganglionated plexus was restimulated.

Table 1. Cardiovascular Effects of Electrically Induced Arrhythmias

		Ventricular Rate (beats/min)			Mean Aortic Pressure (mm Hg)			LV Systolic Pressure (mm Hg)		
Type of Arrhythmia	n	Before	Arrhythmia	p Value	Before	Arrhythmia	p Value	Before	Arrhythmia	p Value
Atrial fibrillation	3	138 ± 6	197 ± 7	0.0005	85 ± 7	77 ± 4	NS	97 ± 5	88 ± 6	NS
Atrial tachycardia	8	139 ± 4	209 ± 8	0.0001	93 ± 3	82 ± 5	0.0001	110 ± 4	101 ± 3	0.0001
AV nodal rhythm	6	126 ± 9	181 ± 6	0.0001	90 ± 4	75 ± 4	0.001	110 ± 8	85 ± 7	0.001
Atrial flutter	1	130	165		97	83		115	107	

Atrial stimulation induced the listed arrhythmias, during which the contractile rate of the ventricles (ventricular rate in beats per minute), mean aortic pressures (in mm Hg) and left ventricular chamber systolic pressures (in mm Hg) were altered.

AV = atrioventricular; LV = left ventricular.

Data Analyses

The rate at which the ventricles were contracting, mean aortic pressures, and peak systolic left ventricular chamber pressures were measured for ten consecutive cardiac cycles, and the mean ± standard error of the mean was calculated. The cardiac responses elicited by atrial pacing were divided into four groups according to the type of arrhythmia generated; in some animals more than one type of arrhythmia developed on repeat atrial stimulation. The cardiac responses elicited in each group were evaluated by comparing the variables measured immediately before each intervention with changes elicited after each intervention. Data obtained before and after atrial stimulations, as well as before and after right atrial ventral ganglionated plexus stimulations during sustained supraventricular tachyarrhythmias, were compared by Student's *t* test.

Results

Generation of Atrial Arrhythmias

Stimulating right atrial tissue of the 8 dogs resulted in various types of dysrhythmias being induced for periods of time lasting 4 minutes or more. Because the right atrium was restimulated several times in each animal, a number of different arrhythmias were induced in the entire group (Table 1). These included atrial fibrillation in 3 animals, atrial tachycardias in 8 animals, various atrioventricular nodal ectopic rhythms in 6 animals, and atrial flutter in 1 animal. During these arrhythmias, ventricular contraction rates were faster than normal and irregular. Lower mean systolic intraventricular and aortic pressures were generated during atrial tachycardias and atrioventricular nodal rhythms (Table 1). In several instances during irregular ventricular contractions, left ventricular systolic pressure was so low that no aortic pressure was generated during many cardiac cycles (Fig 2B). In addition, pulsus alternans was induced in a number of instances, the weaker contraction producing low (Fig 3A) or no (Fig 3B) aortic pressure.

Effects of Right Atrial Ganglionated Plexus Stimulation on Cardiodynamics During Tachyarrhythmias

When the right atrial ventral ganglionated plexus was stimulated in control states, bradycardia was induced. When these stimuli were repeated after cardiac arrhythmias had been induced, the overall rate at which the ventricles contracted was reduced, resulting in an increase in mean aortic pressure. When atrial fibrillation was induced in 3 animals, right atrial ganglionated plexus stimulation reduced ventricular rate. This in turn resulted in a more regular rate of contraction of the ventricles and thus relatively consistent systolic pressure generation in the left ventricular chamber and, therefore, in the aorta (Fig 2B, C).

Atrial tachycardia was induced in all 8 dogs. This was accompanied by a reduction in mean aortic pressure and left ventricular systolic pressure (see Table 1). When the right atrial ventral ganglionated plexus was stimulated during these episodes, heart rate was reduced and left ventricular systolic pressure increased (Table 2). Pulsus alternans also developed during many of these tachycardias. When the right atrial ventral ganglionated plexus was stimulated during pulsus alternans, in every instance each cardiac cycle generated aortic pressures of relatively similar magnitude (Figs 2A, 3).

In 6 dogs, a fast atrioventricular nodal rhythm developed during and after stimulation of right atrial tissue. In these instances, right atrial ventral ganglionated plexus stimulation induced ventricular slowing throughout the period of stimulation so that mean aortic pressure increased. Pulsus alternans was also produced in 4 of these dogs during fast atrioventricular nodal rhythms (Fig 3A). This was consistently converted to a normal contractile pattern when the right atrial ventral ganglionated plexus was stimulated (Fig 3B). In the one case of induced atrial flutter, right atrial ventral ganglionated plexus stimulation produced slower and more regular ventricular contractile rates. In that animal, heart rate was slowed (165 to 123 beats per minute) and mean aortic pressure increased (85 to 92 mm Hg). After atropine administration, no slowing of heart rate was induced when the atrial ganglionated plexus was stimulated.

Comment

The occurrence of supraventricular tachycardias after open heart operations in adults is common [1], particularly in older male patients [10]. Its etiology are unknown. Supraventricular tachycardia commonly occurs 2 days

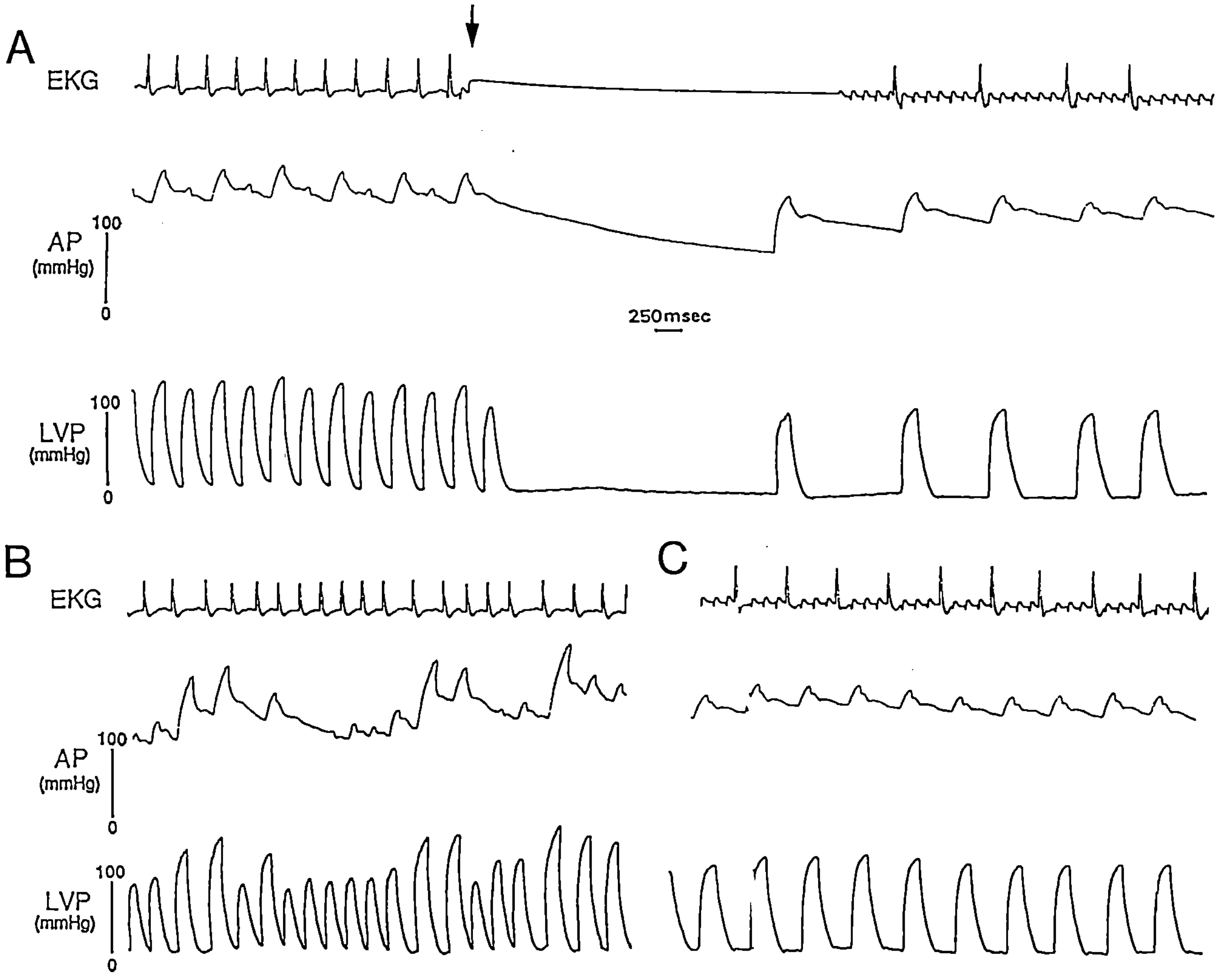

Fig 2. (A) Effects of right atrial ventral ganglionated plexus stimulation (arrow *denotes start of stimulation) on cardiodynamics during induced atrial tachycardia. The pulsus alternans accompanying the tachycardia was converted, after a period of asystole, to a state in which every ventricular contraction generated aortic pressure of relatively similar magnitude. (B) Atrial fibrillation was induced in another animal, resulting in irregular aortic and left ventricular pressure systolic pressure generation. (C) When the right atrial ganglionated plexus of the animal used to illustrate panel B was stimulated, ventricular and aortic pressure generation became relatively consistent.* (AP = *aortic pressure;* LVP = *left ventricular chamber pressure.)*

after operation and has been attributed to a direct inflammatory response [10]. This was certainly a contributing factor in the genesis of electrically induced supraventricular tachycardia in the present investigation and in that reported by Pagé and colleagues [9].

Although supraventricular tachycardia is generally treated pharmacologically, intubation and cardioversion is required in patients in whom unstable hemodynamics develop during this state. Although most patients respond transiently to agents that slow heart rate, perma-

Table 2. Effects of Right Atrial Ganglionated Plexus Stimulation

		Ventricular Rate (beats/min)			Mean Aortic Pressure (mm Hg)		
Type of Arrhythmia	n	Before	Stimulation	*p* Value	Before	Stimulation	*p* Value
Atrial fibrillation	3	197 ± 7	122 ± 6	0.0005	77 ± 4	84 ± 9	0.0005
Atrial tachycardia	8	209 ± 8	145 ± 5	0.0001	82 ± 5	90 ± 4	0.0001
AV nodal rhythm	6	181 ± 6	138 ± 8	0.0001	75 ± 4	88 ± 7	0.001
Atrial flutter	1	165	123		83	92	

Stimulation of the right atrial ventral ganglionated plexus during each of the arrhythmia phases shown in Table 1 resulted in changed ventricular contractile rates and mean aortic pressures.

AV = atrioventricular.

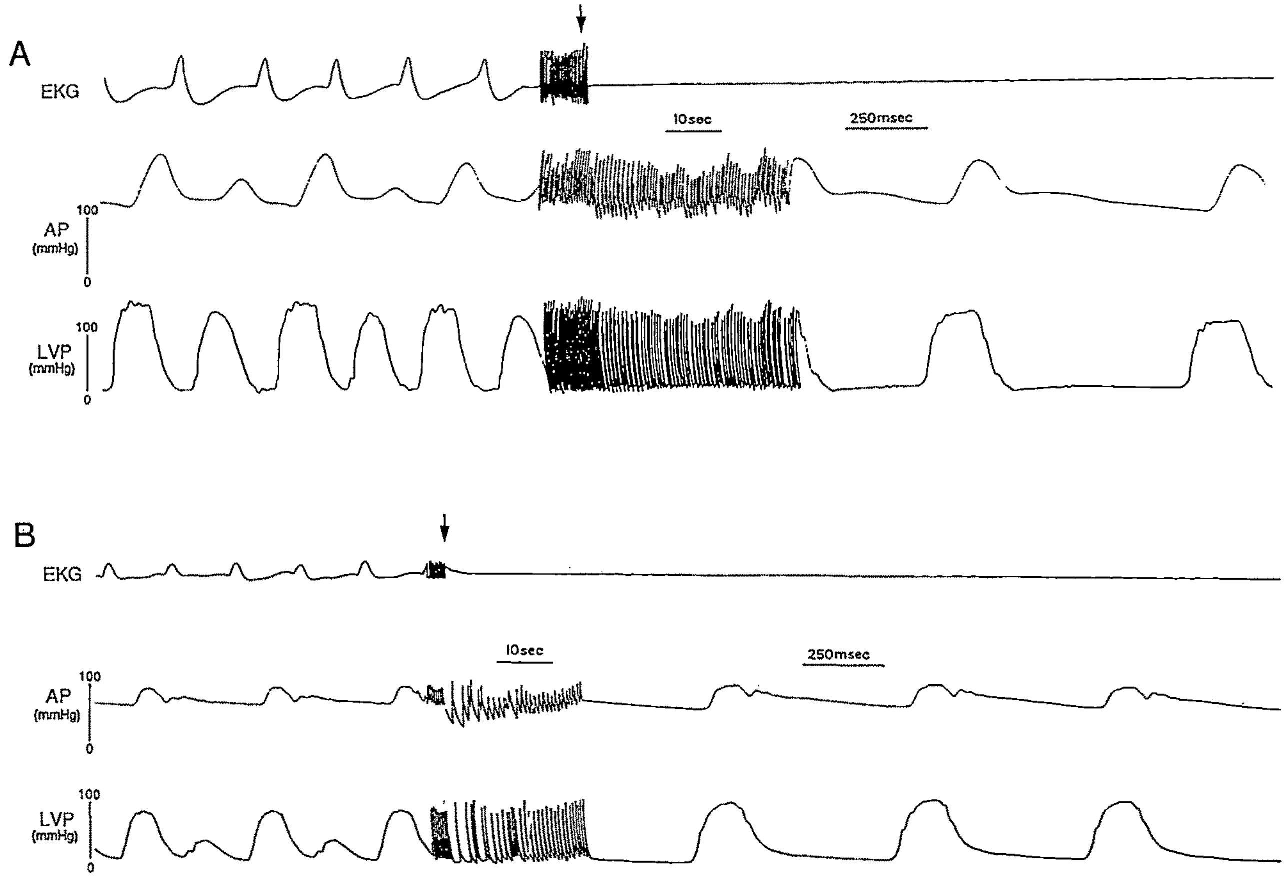

Fig 3. (A) Supraventricular tachycardia induced in another animal, resulting in pulsus alternans. When the right atrial ganglionated plexus was stimulated (arrow, *top), ventricular rate was slowed and aortic pressure generation became regular. (B) During a supraventricular tachycardia induced in another animal, pulsus alternans was induced so that every second systole did not generate aortic pressure. When the right atrial ventral ganglionated plexus was stimulated* (arrow, *top of panel), ventricular contractile rate was slowed and then every ventricular contraction resulted in relatively consistent aortic pressure generation.* (AP = *aortic pressure;* LVP = *left ventricular chamber pressure.)*

nent cardioversion to sinus rhythm may take several days. We investigated whether direct electrical stimulation of atrial ganglionated plexi known to contain vagal efferent neural elements could modify the ventricular rate in sedated dogs during control conditions as well as during supraventricular tachyarrhythmias. Ganglionated plexi have been identified in collections of fat on the ventral surface of canine atria [3] and ventricles [7]. Electrical stimulation of discrete loci in these ganglionated plexi can elicit cardiac responses, including bradycardia [4]. These loci occur most consistently in an area just anterior (ventral) to the right superior pulmonary vein, an area that is widely divided when the mitral valve is exposed by a right interatrial groove incision in humans.

In the present study, different types of atrial arrhythmias were produced in all dogs using the protocol described by Pagé and colleagues [9]. In all animals, atrial and ventricular rhythm became regular when the right atrial ventral ganglionated plexus was stimulated. Electrical stimulation of the right atrial ganglionated plexus modified ventricular rate both before and after tachycardias were induced. In addition, ventricular performance, as measured by mean aortic pressure, during these tachycardias was improved. The effects on heart rate induced by neural stimulations presumably resulted from activation of efferent parasympathetic neural elements because the responses were not elicited after atropine administration. The main right vagosympathetic complex is accessible in humans behind the superior vena cava [11]. Because most cardiac branches leave this complex cephalad to the heart, stimulating this structure at the level of the heart presumably would yield varying cardiac responses. If cardiac vagal efferent neural elements are located adjacent to the right superior pulmonary vein in humans, it may be possible to stimulate these cardiac ganglionated plexi in humans to manage postoperative supraventricular tachycardias.

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Pulmonary circulation - advances and controversies

edited by **C.A. Wagenvoort** *and* **H. Denolin**

The Working Group of Pulmonary Hypertension of the International Society and Federation of Cardiology was formed in Prague in 1984. It was decided then to include in its aims the preparation of reviews and comments and the identification of controversies regarding the pulmonary circulation and pulmonary hypertension in particular. Implementation of this commitment, however, appeared quite difficult and it was decided that the task of the Working Group should be realized in the form of a book.

This book focuses on a number of topics within the field of the pulmonary circulation in which there have been recent advances or important developments, or in which controversial issues are at stake.

It will no doubt serve not only as an up-to-date source of information but also as a stimulus for further research to cardiothoracic surgeons, paediatricians, anaesthesiologists, intensive care physicians and pathologists, as well as cardiologists and pulmonologists.

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Systemic Arterial Air Embolism in Penetrating Lung Injury

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Systemic arterial air embolism is frequently unrecognized as a cause of death among patients with isolated penetrating lung injury. Between 1975 and 1983 at Parkland Memorial Hospital, the complication of systemic arterial air embolism developed in 9 patients with penetrating lung injury (six gunshots and three stabbings). Eight patients were either in profound shock or experienced cardiac arrest and all were intubated and on positive-pressure ventilation, frequently on a manual resuscitator bag before or at the time of diagnosis. The diagnosis was made by direct visualization of air in the coronary vessels in all 9 patients, and in 3 air was also aspirated from the left ventricular apex and aortic root. In addition, 5 patients had clinically significant hemoptysis. At operation, only an isolated injury to the lung was found in 7 of the 9 patients. Arterial air embolism is a highly lethal complication; 6 of our patients died, a mortality rate of 66%. Thus, it clearly behooves us to be more alert to the possible occurrence of this complication among all victims of penetrating chest trauma. We must accept that systemic arterial air embolism is an established complication of penetrating lung injury and must recognize that it occurs much more frequently than has been previously reported. Prompt diagnosis coupled with aggressive efforts at cardiopulmonary resuscitation is crucial for successful management of patients with air embolism.

(Ann Thorac Surg 1990;50:257–61)

Systemic arterial air embolism as a complication of penetrating lung injury is a relatively recent observation. Its acceptance as a specific clinical entity has been very slow in coming, a situation not too dissimilar from what took place at the turn of the century regarding a little-known entity called "pleural shock" syndrome. Pleural shock, as originally described by Roger in 1864 [1], was characterized by the sudden onset of hemodynamic collapse, seizures, and, at times, sudden death occurring as a complication of thoracentesis, therapeutic pneumothorax, and pulmonary resection [1–4]. Initially, this phenomenon was attributed to cardioinhibitory or vasomotor effects and other so-called pleural reflexes, which were somehow triggered by invasive procedures involving the pleural cavity [3, 4]. Subsequently, air embolism was suspected to be the underlying mechanism. The clinical report by Brandes [5] and the later animal experiments by Van Allen and co-workers [6] and Moore and Braselton [7] established the definitive relationship between systemic arterial air embolism and the phenomenon of pleural shock.

Reports of air embolism complicating penetrating lung injury have appeared in the literature only in the past two decades. To our knowledge, no case has been reported in any of the major wars of this century. In 1966, Chiu and associates [8] were first to confirm the occurrence of coronary artery air embolism in the presence of lung injury in an animal experiment in which a dog's lungs were lacerated and ventilated with high (40 mm Hg) intrabronchial pressure. In 1973, Thomas [9] published the first clinical report of 4 patients with penetrating lung injury in whom this complication developed. This report caused skepticism and stimulated controversy in many trauma centers in this country, including our own; however, subsequent laboratory investigations and clinical experiences [9, 10] confirmed the earlier observations of Chiu and Thomas. The recent autopsy study by King and associates [11] conclusively documented the occurrence of this complication; these investigators even suggested that systemic arterial air embolism may frequently be the cause of death among patients with isolated penetrating lung injury.

Between 1975 and 1983 at Parkland Memorial Hospital, one of us (A.S.E.) personally managed 9 patients in whom systemic arterial air embolism developed after penetrating lung injury. This report retrospectively analyzes this group of patients.

Clinical Experience

Before 1975, we were skeptical, as were many other investigators, that systemic air embolism could complicate pulmonary injury. In 1975, however, our skepticism ended when a young man was admitted to the emergency department with a gunshot wound to the left chest. Resuscitation, including emergency department thoracotomy, was unsuccessful. During resuscitation, however, localized crepitation was palpable deep in both groins. Although this was initially believed to be subcutaneous emphysema, needle aspiration revealed air in the femoral

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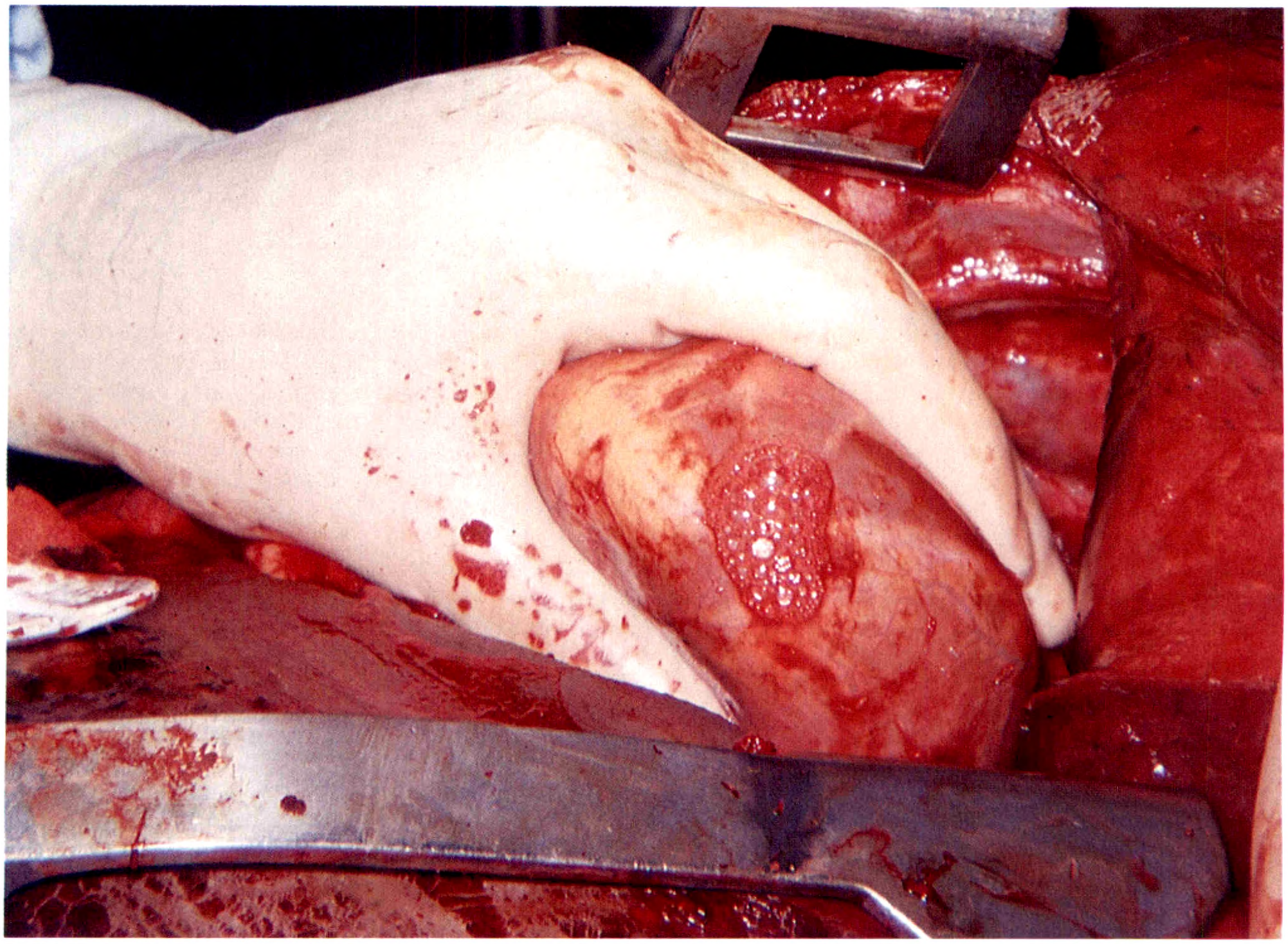

Fig 1. A massive amount of air has been aspirated from the left ventricle. Bubbles of air are evident leaking through the left ventricular needle-punctured site.

arteries. Systemic arterial air embolism was confirmed by visualization of air in the coronary vessels and by aspiration of a large volume of air from the left ventricular apex and aortic root (Fig 1). Vigorous air leak with foamy air-blood admixture exuding from both the entry and exit wound of the left upper lobe of the lung was also noted; this was the only clinically significant injury found. It was evident that the patient died of massive systemic arterial air embolism. After this incident, concerted efforts were made to diagnose this complication among victims of penetrating chest injury. During the ensuing 8-year period, 8 additional patients were examined by one of us (A.S.E.). The clinical summaries of these cases are presented in Table 1.

The patients ranged in age from 15 to 42 years; 6 sustained gunshot wounds and 3 sustained knife wounds. Three patients who arrived in the emergency department without vital signs and with cardiopulmonary resuscitation in progress had thoracotomy performed there. Five patients were in profound shock and were rushed to the operating room; only 1 patient was in stable condition on arrival, and he required an urgent thoracotomy for massive hemothorax.

All patients were intubated and on positive-pressure ventilation, frequently with a manual resuscitator bag, at the time the diagnosis of systemic air embolism was made. At operation, every patient had either a deep puncture wound or a through-and-through wound of the lung in close proximity to the hilum. In 7 of the 9 patients, the lung injury was the only clinically significant finding. Of the other 2, 1 patient had a superficial avulsive-type laceration of the lateral wall of the left ventricle and the other had a thoracic spinal cord injury (T-4 level). Five patients had massive amounts of blood suctioned from the endotracheal tube, severely compromising mechanical ventilation. In every patient, the diagnosis of air embolism was made by direct visualization of air in the coronary vessels; in 3 patients, a large volume of air was also aspirated from the left ventricular apex and aortic root. In 4 patients, vigorous air leaks with blood exuding from the wound or wounds of the lung were noted. Four patients survived the operation; 3 were discharged with complete recovery, and 1 died a week later with severe neurological deficit.

Comment

The incidence of systemic air embolism complicating penetrating lung injury remains obscure for several reasons. First, the clinical manifestations of systemic air

Table 1. Air Embolism Complicating Penetrating Lung Injury (Parkland Memorial Hospital, 1975–1983)

Patient No.	Age (yr)	Sex	Type of injury	Clinical Presentation	Operative Procedure and Findings	Diagnosis	Outcome
1	34	M	GSW (L) chest	Agonal, shock, massive hemothorax	EDT (anterior); through-and-through wound of LUL with vigorous air leak	Air in coronary vessels; air aspirated from femoral arteries, LV apex, and aortic root	Died
2	22	M	GSW (L) chest	Hypotensive, massive hemothorax: sudden cardiac arrest	Left posterolateral thoracotomy; deep wound of LUL; blood in endotracheal tube	Air in the coronary vessels; air aspirated from LV apex and aortic root	Died
3	14	F	GSW (L) chest	Agonal, shock, massive hemothorax	EDT (anterior); through-and-through wound LLL; blood in the endotracheal tube	Air in coronary vessels	Died
4	24	M	GSW (R) chest	Hypotensive, massive hemothorax; stabilized with volume replacement; sudden cardiac arrest	Right posterolateral thoracotomy; through-and-through wound RUL with large air leak and bleeding from the wounds; RUL lobectomy	Air in coronary vessels	Survived; discharged
5	18	M	SW (L) chest	Hypotensive, massive hemothorax; stabilized with volume replacement; sudden cardiac arrest	Left posterolateral thoracotomy; substantial amount of blood in endotracheal tube with difficulty of ventilation; deep puncture wound LLL; LLL lobectomy	Air in coronary vessels	Survived; discharged
6	28	F	GSW (L) chest	Stable; massive hemothorax; proximity to the heart; sudden cardiac arrest	Left anterior thoracotomy; avulsive wound in the lateral LV; through-and-through wound LUL with vigorous air leak; LUL lobectomy	Air in coronary vessels	Survived operation, but died with severe neurological deficit
7	24	M	SW (L) chest	Hypotensive; tension hemopneumothorax; sudden cardiac arrest	EDT (anterior); deep laceration LUL with vigorous air leak	Air in coronary vessels	Died
8	28	F	SW (L) chest	Hypotensive; massive hemothorax; T-4 level paraplegia; sudden cardiac arrest	Median sternotomy; deep puncture wound LUL; blood in endotracheal tube	Air in coronary vessels; air aspirated from LV apex and aortic root	Died
9	42	M	GSW (R) chest	Hypotensive; massive hemothorax; proximity to the heart	Median sternotomy; through-and-through wounds of middle lobe with vigorous air leak and bleeding; blood in endotracheal tube; RML lobectomy	Air in coronary vessels	Survived; discharged

EDT = emergency department thoracotomy; GSW = gunshot wound; LUL = left lower lobe; LV = left ventricular; RML = right middle lobe; RUL = right upper lobe; SW = stab wound.

embolism are so insidious and nonspecific that the diagnosis is rarely suspected in a seriously injured patient. Second, the diagnosis is usually made only on direct visualization of air in the coronary vessels or by aspiration of air from the left ventricle or great vessels; therefore, it is usually made only at the time of thoracotomy. Third, there is still no standard postmortem method for definitive diagnosis of this entity. It is to be hoped that the technique used by King and associates [11] will be adopted by other forensic pathologists and will improve our overall diagnostic capability.

After a penetrating chest injury, air has the potential to gain access to either the systemic venous or arterial circulation. Systemic venous air embolism was reported as the possible cause of death in a patient who sustained a gunshot wound to the chest. In this patient, the surgeons theorized that a massive amount of air from an associated pneumothorax entered the venous circulation through a severed subclavian vein [12]. Apart from this single patient, there have been no other similar reports. Thus, in penetrating lung injury, the major concern regarding air embolism must be focused on interruption of the systemic arterial circulation, most specifically the coronary circulation.

The traumatic creation of a serious bronchopulmonary venous fistula is the primary underlying mechanism in the development of this complication. The deep puncture stab wounds and through-and-through bullet wounds in close proximity to the hilum seen in our patients are the types of injury that create and maintain a sizable fistulous communication between the proximal bronchus and a pulmonary vein. Unlike the pulmonary artery, which is in close proximity to its accompanying bronchus along its entire course, the pulmonary vein is in close proximity to its bronchus only in the hilar region. Detailed anatomical dissections of the lung specimen were performed in 6 of our cases, and in 3 a fistulous communication was clearly demonstrated. In 3 others, the missile tract could be demonstrated to have served as the conduit between the openings in the bronchus and pulmonary vein. The presence of a fistula coupled with high positive-pressure ventilation favors movement of air from the bronchus into the pulmonary vein and then into the left atrium and the systemic arterial circulation. In addition to this anatomical feature, however, other factors, such as hemodynamic status and pressure gradient between the bronchus and pulmonary vein, are very important. In these seriously injured trauma victims, hypotension, hypovolemia, and positive-pressure ventilation create a favorable environment for development of this complication.

The role of positive-pressure ventilation in the development of traumatic systemic air embolism is well established [8, 13, 14]. Animal experiments demonstrate that during normal ventilation (inspiratory pressure of 10 to 20 mm Hg), pulmonary venous pressure is higher than intrabronchial pressure. During mechanical ventilation with inspiratory pressure up to 40 mm Hg, pulmonary venous pressure increases even more as a consequence of intrathoracic pressure transmission [8]. In the presence of a bronchus to pulmonary venous communication, this pressure differential tends to favor movement of blood from the pulmonary vein into the bronchial tree and thus explains the onset of intrabronchial bleeding or hemoptysis that frequently occurs in these patients. When the ventilating pressure exceeds 40 mm Hg, however, the intrabronchial pressure increases above pulmonary venous pressure, reversing the existing pressure gradient between these two structures. This time, the pressure change allows movement of air into the pulmonary vein and into the left side of the heart. This high inspiratory pressure is easily achieved, especially during resuscitation. Direct measurements of inspiratory pressure among trauma victims during resuscitation have recorded pressures as high as 100 mm Hg [13]. This exceedingly high ventilating pressure may also explain why body position does not appear to influence the occurrence of this complication. In our series, we observed this complication during a standard posterolateral thoracotomy (straight lateral position), a median sternotomy (supine position), and an anterior thoracotomy (45-degree lateral position).

Unlike massive air embolism complicating cardiopulmonary bypass procedures, in which the immediate concern is in the interruption of cerebral blood flow and resultant brain damage, the primary concern with systemic arterial air embolism complicating a penetrating lung injury is in the interruption of the coronary blood flow and resultant myocardial injury. The effects of even small amounts of air in the coronary circulation are well known [15]. For patients to survive this catastrophic event, it is imperative that the diagnosis be made promptly and the source of air emboli be interrupted immediately.

Several clinical features should alert the surgeon to this complication: (1) a sudden hemodynamic collapse, usually with ventricular fibrillation, in a previously stable patient; (2) hemoptysis or recovery of blood with endotracheal tube suctioning; (3) the presence of a vigorous air leak with foamy air-blood admixture exuding from the wound or wounds of the lung; and (4) the sudden onset of seizures.

Once the diagnosis is suspected, the hilum or pedicle of the involved lung or lobe must be clamped immediately. This maneuver, interrupting the source of air emboli, is the single most important therapeutic maneuver. Diagnosis is confirmed by exposure of the heart and careful inspection of the coronary vessels for the presence of air bubbles while vigorous cardiac massage is initiated. This is the one rare event in trauma care for which evaluation and resuscitation must be performed simultaneously. Subsequently, a series of critical maneuvers designed to facilitate rapid removal of air from the coronary circulation is started. Ventilatory pressure is decreased, ventilation is maintained with 100% oxygen, and the patient is placed in a steep head-down position. Vigorous cardiac massage is continued while proximal aortic hypertension is induced by manual occlusion of the ascending or descending aorta as recommended by Geohegan and Lam [16]. The left ventricular apex and aortic root are then aspirated; sometimes, even direct needle puncture of the coronary arteries is used to facilitate removal of air.

After these measures have been taken, cardiac rhythm is restored by defibrillation, and adequate blood pressure is maintained by infusion of vasopressors as needed. Definitive lung resection, frequently lobectomy, is then performed while the hilum remains clamped.

In the recovery period, as with any other form of systemic arterial air embolism, the main concern is the status of the patient's cerebral function. Although none of our 3 long-term survivors had any serious neurological deficit, Yee and associates [17] reported that a few of their patients indeed had some neurological sequelae that resolved with time. It is our impression that when cerebral circulation is seriously interfered with by air emboli complicating penetrating lung injury, the embolism is so massive that it is probably incompatible with life. Indeed, 1 of our patients who survived the immediate postoperative period died a week later, having failed to recover from a severe neurological deficit.

As described by other investigators and confirmed in this report, the highly lethal complication of thoracic trauma, air embolism, often occurs among patients with isolated, easily repairable lung injuries. It behooves us to be even more cognizant of the occurrence of this complication. At present there should be no more doubts as to the existence of the clinical entity of systemic arterial air embolism complicating a penetrating injury to the lung. In fact, we can assume that this complication occurs much more frequently than was previously reported, and that only conscious efforts on the part of physicians involved in the management of chest trauma are necessary for prompt diagnosis and salvage of these patients.

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The Concentration of Calcium in Neonatal Cardioplegia

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The optimal calcium concentration in cardioplegia for the newborn has not been determined. Therefore, the effect of 0, 0.6, 1.2, 1.8, and 2.4 mmol/L calcium in modified St. Thomas cardioplegia was evaluated in isolated working hearts of 7- to 10-day-old rabbits. Functional recovery was determined by comparing aortic flow, developed pressure, and first derivative of left ventricular pressure (dP/dt) before and after 1 hour of normothermic (37°C) ischemia. As percentages of baseline values, recovery of developed pressure and dP/dt averaged 10% ± 1% (mean ± standard error of the mean) and 10% ± 1% with 0 mmol/L, 46% ± 7% and 44% ± 8% with 0.6 mmol/L, 79% ± 2% and 76% ± 2% with 1.2 mmol/L, 67% ± 2% and 61% ± 5% with 1.8 mmol/L, and 65% ± 5% and 65% ± 7% with 2.4 mmol/L calcium, respectively. Significant improvement in recovery of developed pressure and dP/dt was detected when the calcium concentration was increased from 0 to 0.6 mmol/L and from 0.6 to 1.2 mmol/L, but the groups with 1.2, 1.8, and 2.4 mmol/L did not differ from one another significantly in terms of developed pressure and dP/dt recovery. There was no recovery of aortic flow when 0 mmol/L calcium was used; at calcium concentrations of 0.6, 1.2, 1.8, and 2.4 mmol/L, recovery of aortic flow averaged 16% ± 7%, 63% ± 10%, 23% ± 10%, and 36% ± 11% of baseline values, respectively. Recovery of aortic flow with 1.2 mmol/L calcium was significantly higher than at concentrations of 0.6 and 1.8 mmol/L. In the rabbit exposed to normothermic ischemia, we conclude that neonatal cardioplegia requires calcium to be effective and that 1.2 mmol/L represents the optimal calcium concentration for the best combination of recovery in aortic flow and developed pressure.

(Ann Thorac Surg 1990;50:262–7)

Vascular conduits, suture material, surgical instrumentation, and technical expertise have improved dramatically over the last three decades, as surgeons accumulated experience in performing procedures to repair congenital cardiac defects. Myocardial protection in the neonate, however, remains a critical problem. Cardioplegic solutions and techniques that may be effective in the adult do not always provide equivalent protection for the immature heart.

The objective of the present study was to focus on a specific component of neonatal cardioplegia, the concentration of calcium, to determine how it may influence functional recovery after a standardized episode of global ischemia. Under normal conditions, fluctuations in intracellular calcium enable contraction to occur, modulate the strength of contraction, and play a role in many other aspects of cell function. Calcium can also be a mediator of biochemical, structural, and functional damage during and after ischemia [1, 2]. To minimize injury produced by calcium during ischemia or reperfusion, subphysiological calcium concentrations have been used in cardioplegia solutions [3, 4]. This strategy is constrained, however, by the requirement for some calcium to maintain structural integrity of myocardial cells [2]. In addition, if calcium concentrations below a critical level are used, the "calcium paradox" and associated severe injury [5, 6] may occur during reperfusion. Thus, both the potential benefits and dangers of calcium must be considered when cardioplegic solutions are designed.

The specific objective of the present study was to determine the optimal calcium concentration in cardioplegia for neonatal myocardium. Experiments were conducted in isolated neonatal rabbit hearts in which cardioplegic solutions containing different concentrations of calcium were administered. Relative recoveries of developed pressure (DP), first derivative of left ventricular pressure (dP/dt), and aortic flow after 60 minutes of normothermic ischemia were used to determine the most beneficial calcium concentrations in cardioplegia.

Material and Methods

The experimental preparation used in this study has been described previously [7–9]. We studied the hearts from New Zealand White rabbits, aged 7 to 10 days (weighing 75 to 150 g). The animals were killed, and the heart and lungs were rapidly excised en bloc and placed in a 4°C physiological saline solution (PSS). The aorta was cannulated to enable establishment of retrograde (or Langen-

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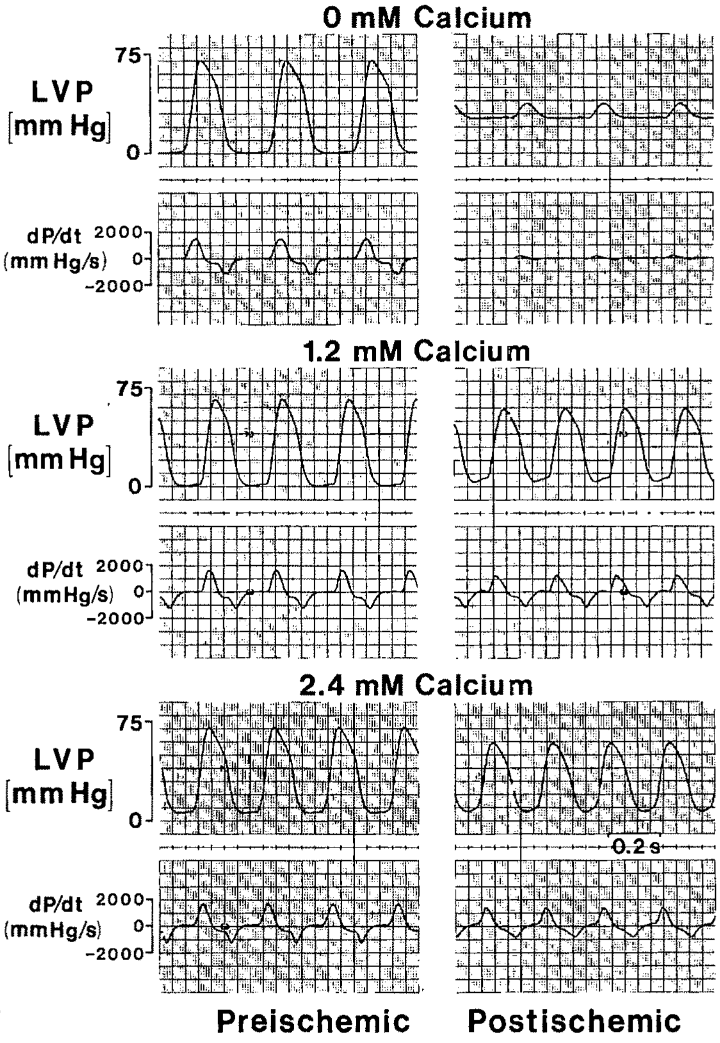

Fig 1. Analog tracings of left ventricular pressure (LVP) and its first derivative (dP/dt) from three experiments to demonstrate the appearance of waveforms derived from the high-fidelity micromanometers (model SPR 249, Millar Instruments) used in this study. The tracings illustrate typical findings before and after normothermic ischemic periods during which cardioplegia containing different concentrations of calcium was infused. The best recovery was evident with 1.2 mmol/L of calcium; the worst recovery was with acalcemic cardioplegia; LVP and dP/dt tended to be lower with 2.4 mmol/L of calcium in cardioplegia than with 1.2 mmol/L of calcium.

dorff) perfusion at an aortic pressure of 55 cm H_2O (approximately 40 mm Hg). The PSS contained (in millimoles per liter) NaCl, 118; $NaHCO_3$, 25; KH_2PO_4, 0.66; KCl, 4; $MgCl_2$, 1.2; $CaCl_2$, 2.4; and dextrose, 11.1. The PSS was equilibrated with 95% oxygen and 5% CO_2 with a pH of 7.4 at 37°C; it was filtered through a 3-μm filter (model AP25, Millipore, Bedford, MA). The oxygen tension of the perfusate was maintained above 600 mm Hg by continuous oxygenation of the reservoir containing PSS.

The heart was perfused in retrograde fashion and remained in the "nonworking" mode for 10 minutes after the aorta was cannulated. During this time, the pulmonary veins were ligated and a cannula was secured in the left atrium. Then the heart was converted to the "working" mode by clamping the aortic inflow line (stopping retrograde perfusion) and opening the aortic ejection and atrial inflow lines, similar to methods described originally by Neeley and colleagues [10] and later modified by Hearse and co-workers [11]. The atrial inflow reservoir was positioned 20 cm above the heart and the heart ejected into a column of PSS 55 cm in height. The heart was bathed in PSS at 37°C in a glass organ bath. Temperatures were continuously monitored with a thermistor probe (Yellow Springs Instrument, Yellow Springs, OH) on the surface of the heart.

After the hearts were maintained in the working (or ejecting) mode for 30 minutes, baseline measurements were obtained. Aortic flow and coronary flow were measured by timed collections from the aortic ejection column and right ventricular effluent, respectively. After flows were calculated, left ventricular pressure was measured by threading a miniature (3F) catheter-mounted micromanometer (model SPR 249, Millar Instruments, Houston, TX) through the left atrial inflow cannula and mitral valve into the left ventricle. Analog tracings of left ventricular pressure and its first derivative were recorded on a pressurized ink chart recorder (model 2600S, Gould Instruments, Cleveland, OH). Examples of tracings from three experiments are shown in Figure 1. Peak systolic pressure, end-diastolic pressure, DP (difference between peak and end-diastolic pressure), and peak positive dP/dt were measured. Following our usual conventions [9], data were not used if the hearts were characterized by DPs less than 40 mm Hg, aortic flow less than 7 mL/min, and coronary flow less than 4 mL/min or greater than aortic flow.

Table 1. Preischemic Hemodynamic Data[a]

Variable	Calcium Concentration (mmol/L) 0	0.6	1.2	1.8	2.4	*p* Value[b]
n	8	11	10	11	10	
LVSP (mm Hg)	68 ± 2	69 ± 1	70 ± 2	68 ± 2	69 ± 2	NS
LVEDP (mm Hg)	4 ± 1	6 ± 1	3 ± 1	4 ± 1	4 ± 1	NS
DP (mm Hg)	64 ± 3	64 ± 2	67 ± 2	64 ± 2	65 ± 2	NS
(+)dP/dt (mm Hg/s)	1,569 ± 97	1,557 ± 53	1,755 ± 77	1,650 ± 66	1,565 ± 91	NS
AF (mL/min)	21 ± 1	22 ± 1	20 ± 1	19 ± 3	21 ± 1	NS

[a] Data are reported as mean ± standard error of the mean. [b] Determined by analysis of variance across groups.

AF = aortic flow; DP = developed pressure; (+)dP/dt = peak positive first derivative of left ventricular pressure; LVEDP = left ventricular end-diastolic pressure; LVSP = left ventricular systolic pressure; NS = not significant.

When baseline measurements were completed, the aortic and left atrial lines were clamped to render the heart globally ischemic and the hearts were perfused retrograde for 5 minutes with St. Thomas cardioplegia containing different concentrations of calcium. The hearts were ischemic for 60 minutes. Myocardial surface temperature was maintained at 37°C by suspending the heart within a thermostatically controlled organ bath. The hearts did not contact any solutions within the organ bath. A second 5-minute infusion of cardioplegia was delivered beginning 30 minutes after the start of the ischemic period. At the end of the 60 minutes of ischemia, the hearts were reperfused in retrograde fashion with PSS for 10 minutes and were then converted to the working mode for 30 minutes. At the end of this period, functional measurements were repeated for comparison with baseline values.

Five different groups were evaluated. In each, the St. Thomas cardioplegia was modified to contain either 0 (n = 8), 0.6 (n = 11), 1.2 (n = 10), 1.8 (n = 11), or 2.4 (n = 10) mmol/L calcium. The pH of the solutions was adjusted to 7.4 with 0.1 N HCl before they were infused. The calcium concentrations were verified with atomic absorption spectrometry. Acid-washed glassware and tubing were used for acalcemic experiments.

Data are mean ± standard error of the mean. Paired *t* tests were used to compare baseline with recovery data within each of the five groups. Analysis of variance was used to compare differences across groups. When significant *F* values were obtained, the Scheffé test was used to discriminate which groups differed from each other.

Animals received care according to the "Principles of Laboratory Animal Care" of the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences (NIH publication No. 80-23, revised 1978). This study was part of a project approved by the University Committee on Use and Care of Animals at the University of Michigan (approval number 1748).

Results

Preischemic and postischemic pressure and flow measurements are summarized in Tables 1 and 2. Single-factor analysis of variance of preischemic DP, end-diastolic pressure, dP/dt, and aortic flow confirmed that baseline function was not significantly different among the five experimental groups (Table 1). After 60 minutes of normothermic ischemia, significant changes were noted in all parameters at each calcium concentration (Table 2). End-diastolic pressures increased significantly in all five groups. The largest increase was in the group with no calcium. There were no significant differences in postischemic end-diastolic pressures among the groups receiving 0.6, 1.2, 1.8, and 2.4 mmol/L calcium (Table 2).

Table 2. Postischemic Hemodynamic Data

Variable	Calcium Concentration (mmol/L) 0	0.6	1.2	1.8	2.4	*p* Value[a]
n	8	11	10	11	10	
LVSP (mm Hg)	30 ± 2[b]	47 ± 2[b]	61 ± 2	55 ± 3	56 ± 3	<0.001
LVEDP (mm Hg)	24 ± 1[b]	17 ± 2	9 ± 1	12 ± 2	11 ± 2	<0.001
DP (mm Hg)	6 ± 1[b]	31 ± 4[b]	52 ± 2	43 ± 2	45 ± 4	<0.001
(+)dP/dt (mm Hg/s)	156 ± 20[b]	732 ± 134[b]	1,315 ± 68	1,018 ± 90	1,010 ± 140	<0.001
AF (mL/min)	0[a]	4 ± 2[a]	12 ± 2	5 ± 2[b]	8 ± 2	<0.001

[a] Determined by analysis of variance across groups. [b] $p < 0.05$ as compared with 1.2-mmol/Lm Ca^{2+} category.

AF = aortic flow; DP = developed pressure; (+)dP/dt = peak positive first derivative of left ventricular pressure; LVEDP = left ventricular end-diastolic pressure; LVSP = left ventricular systolic pressure.

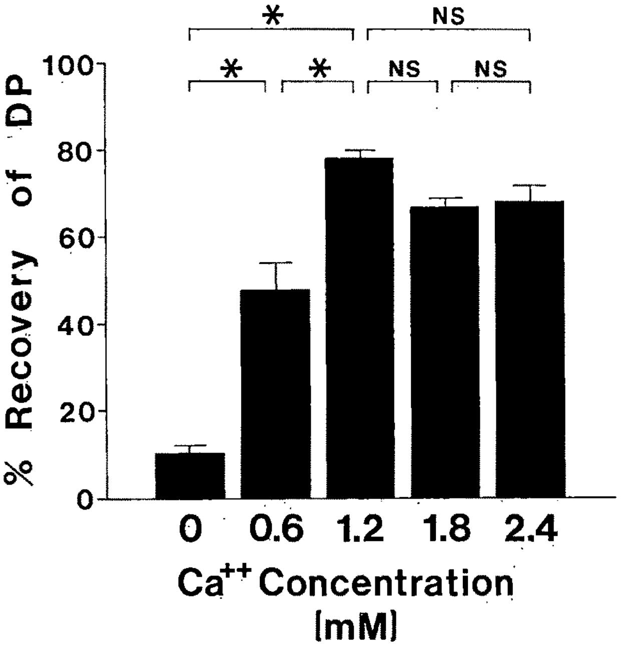

Fig 2. Relative recovery of developed pressure (DP) *after 60 minutes of normothermic ischemia in neonatal rabbit hearts treated with different concentrations of calcium. Data are presented as percentages of baseline values. Recovery averaged 10% ± 1%, 48% ± 6%, 78% ± 2%, 67% ± 2%, and 68% ± 4% in the groups with 0, 0.6, 1.2, 1.8, and 2.4 mmol/L of calcium, respectively. There were no significant differences among the groups with 1.2, 1.8, and 2.4 mmol/L of calcium; the values of the groups with 0 and 0.6 mmol/L of calcium were significantly lower than that of the group with 1.2 mmol/L of calcium. The data indicate that acalcemic cardioplegia provides no benefit during normothermic ischemia in neonatal hearts and suggest that optimum protection is provided by cardioplegia containing at least 1.2 mmol/L of calcium. (** $p < 0.05$; NS = *not significant.)*

Percentage recovery data are shown in Figures 2 through 4. The group with no calcium showed only 10% ± 4% recovery of DP after reperfusion. The group with 0.6 mmol/L of calcium was characterized by significantly better recovery of DP, averaging 48% ± 6% of baseline values. The group with 1.2 mmol/L of calcium was associated with recovery of DP (78% ± 2%) that was significantly better than the results of the groups with 0 and 0.6 mmol/L of calcium. Recovery of DP appeared to plateau with the three high calcium concentrations: there were no significant differences between the calcium concentrations of 1.2 and 1.8 mmol/L (67% ± 2%) or 1.8 and 2.4 mmol/L (68% ± 4%) (Fig 2).

The effects of different calcium concentrations in cardioplegia on recovery, defined in terms of dP/dt, are shown in Figure 3. Percentage recovery averaged 10% ± 1%, 46% ± 8%, 75% ± 2%, 61% ± 4%, and 63% ± 7% in the groups with 0, 0.6, 1.2, 1.8, and 2.4 mmol/L of calcium, respectively. Recovery of dP/dt in the group with 0.6 mmol/L of calcium significantly exceeded recovery in the group with no calcium. Recovery in the group with 1.2 mmol/L of calcium was significantly greater than that in the groups with 0.6 and 0 mmol/L of calcium. There were no significant differences in recovery of dP/dt among the groups with 1.2, 1.8, and 2.4 mmol/L of calcium (Fig 3), similar to the plateau of recovery observed with DP.

The results in terms of aortic flow recovery are summarized in Figure 4. There was no recovery of ejection in the group with no calcium; none of the eight hearts in this group were able to eject after the ischemic period. In the group with 0.6 mmol/L of calcium, five of the 11 hearts ejected and recovery averaged 22% ± 9% of baseline values for the entire group. The most impressive recovery of aortic flow occurred in the group with 1.2 mmol/L of calcium. All 10 hearts in this group ejected after ischemia, and aortic flow averaged 63% ± 8% of baseline, which was significantly higher than that of the groups with 0 and 0.6 mmol/L of calcium. Six of the 11 hearts in the group with 1.8 mmol/L of calcium ejected, and aortic flow recovery (24% ± 8% of baseline) was significantly less than that in the group with 1.2 mmol/L of calcium (Fig 4). Six of 10 hearts in the group with 2.4 mmol/L of calcium ejected. Although recovery averaged only 36% ± 11%, it was not significantly different from the groups with 1.8 or 1.2 mmol/L, given the relatively high variability in the aortic flow data.

Comment

The objective of this study was to determine the effects of altering calcium concentration in cardioplegia on recovery

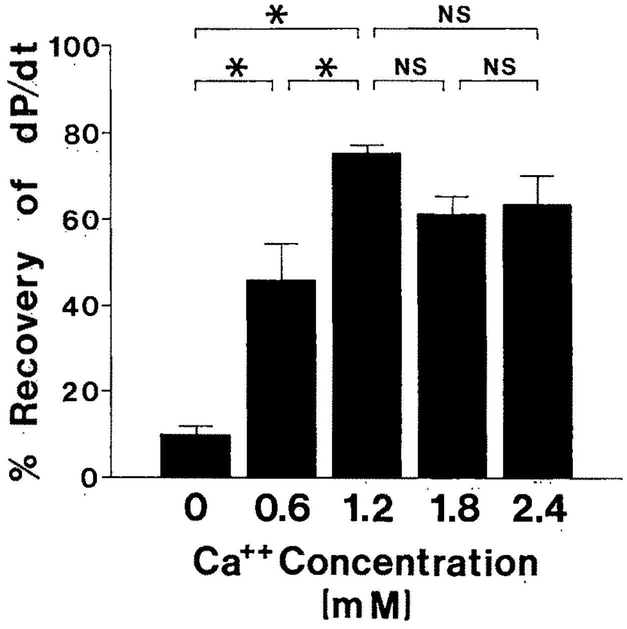

Fig 3. Relative recovery of first derivative of left ventricular pressure (dP/dt) *after 60 minutes of normothermic ischemia in neonatal rabbit hearts treated with cardioplegia containing different concentration of calcium. Data are presented as percentages of baseline values. Recovery of dP/dt averaged 10% ± 1%, 46% ± 8%, 75% ± 2%, 61% ± 4%, and 63% ± 7% in the groups with 0, 0.6, 1.2, 1.8, and 2.4 mmol/L of calcium, respectively. A pattern similar to that observed with developed pressure was observed: The groups with 0 and 0.6 mmol/L of calcium were characterized by significantly lower recovery than that of the group with 1.2 mmol/L of calcium; there were no significant differences among the groups with 1.2, 1.8, and 2.4 mmol/L of calcium. (** $p < 0.05$; NS = *not significant.)*

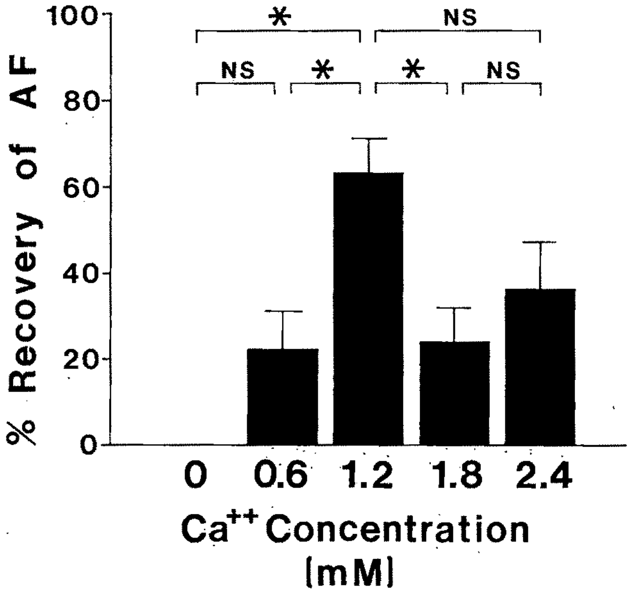

*Fig 4. Relative recovery in aortic flow (*AF*) after 60 minutes of normothermic ischemia in neonatal rabbit hearts treated with cardioplegia containing different concentrations of calcium. Data are presented as percentages of baseline values. Recovery averaged 0%, 22% ± 9%, 63% ± 8%, 24% ± 8%, and 36% ± 11% in the groups with 0, 0.6, 1.2, 1.8, and 2.4 mmol/L of calcium, respectively. In addition to displaying the highest average recovery of aortic flow, the group with 1.2 mmol/L of calcium was the only one in which all hearts ejected after the ischemic period. In the group with no calcium, none of the hearts ejected after ischemia; approximately half of the hearts ejected in the remaining groups. The data suggest that 1.2 mmol/L of calcium is the optimal calcium concentration for neonatal rabbit hearts undergoing normothermic ischemia.* (* $p < 0.05$; NS = *not significant.)*

of left ventricular function in neonatal rabbit hearts. The hearts were exposed to 60 minutes of normothermic ischemia, which results in approximately 30% recovery of DP and no recovery of aortic flow without use of cardioplegia, based on previous findings [9]. In the present study, cardioplegia was beneficial at 37°C only if it contained calcium, and recovery appeared optimal when the concentration was 1.2 mmol/L. Although DP and dP/dt recovered to levels that did not differ significantly when the calcium concentration was 1.2 mmol/L or greater (see Figs 2, 3), the group with 1.2 mmol/L of calcium had the highest recovery of aortic flow (see Fig 4) and was the only group in which all hearts were capable of ejection after ischemia.

The importance and potential dangers of calcium in ischemic and reperfused myocardium have been demonstrated repeatedly [1, 5, 6, 12, 13]. The effect of altering the calcium concentration in cardioplegia was evaluated by Yamamoto and associates [3] in isolated, adult rat hearts. After 35 minutes of normothermic ischemia, recovery of aortic flow was maximal and creatine kinase leakage was minimal when the calcium concentration was 1.2 mmol/L. There was a rapid decrease in protection when the calcium concentration was higher or lower than this value. The results of Yamamoto and associates [3], obtained with a model of normothermic ischemia, appear to contrast with other reports on the salutary effects of acalcemic cardioplegia in adult animals. The disparity may be explained by differences in myocardial temperature during ischemia [3, 4].

Because neonatal and adult hearts differ in many respects [7, 13–19], including sensitivity to calcium-induced injury [20, 21], we hypothesized that the optimum calcium concentration for neonatal cardioplegia also may differ from that of the adult. The results of the present study, however, suggest that 1.2 mmol/L of calcium is the optimal calcium concentration for cardioplegia used during normothermic ischemia in neonatal rabbit hearts, similar to the conclusions of Yamamoto and associates [3], who evaluated normothermic ischemia in adult rats. We acknowledge that the effects of hypothermia, not determined in the present study, could alter the optimal calcium concentration and the potential sensitivity of the myocardium to low calcium concentrations.

The only neonatal study comparable with ours was described in a recent preliminary report by Riva and Hearse [22]. They varied calcium concentration in cardioplegia delivered to isolated neonatal rat hearts during different durations of normothermic ischemia. After 60 minutes of ischemia (the same duration of ischemia we used), altering calcium concentrations in cardioplegia from 0 to 2.4 mmol/L had little effect on recovery of DP, findings that differ from those we made in neonatal rabbits. The different effects of acalcemic cardioplegia on neonatal rabbit (characterized by virtually no recovery of function) and rat hearts (approximately 35% recovery of baseline DP) are particularly striking. Species differences may explain the disparity in part, but additional investigation will be required to explain it more completely.

This study has a number of limitations, and its results must be interpreted with caution as the experimental methods are quite different from those used clinically. Use of an isolated heart model may be criticized for resultant inability to assess the effect of coronary collaterals. Surgical repair in the neonate is most often performed under conditions of circulatory arrest, however, in which collateral circulation would not be a factor. Furthermore, other studies [23] with blood-perfused models have shown results similar to those of our study, in which asanguinous perfusion was used. Finally, although not clinically applicable, ischemia at 37°C was useful in evaluation of the interventions in this study separate and distinct from hypothermia.

In summary, we evaluated the effects of different calcium concentrations in cardioplegia on functional recovery of neonatal rabbit hearts exposed to 60 minutes of normothermic ischemia. Acalcemic cardioplegia was detrimental, resulting in very poor recovery of DP and dP/dt and no recovery of aortic flow, leading us to conclude that calcium is necessary in neonatal cardioplegia under these experimental conditions. The optimal calcium concentration, determined as the concentration associated with the best combination of recovery of DP, dP/dt, aortic flow, and number of hearts ejecting, was 1.2 mmol/L. Increasing the calcium concentration further did not improve pressure-generating capacity and increased the number of nonejecting hearts. Additional investigation will be necessary to determine whether hypothermia alters the manner in which calcium in cardioplegia influences recovery of ventricular function after global ischemia.

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Determinants of Pulmonary Function in Patients Undergoing Coronary Bypass Operations

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Pulmonary function testing was conducted consecutively in 29 healthy men (age range, 42 to 71 years) undergoing elective coronary artery bypass grafting. Lung volumes, expiratory flow rates, diffusing capacity, and blood gases were determined before operation, at discharge (8.7 ± 1.9 days), and at 3 months postoperatively. In addition, peak expiratory flow rate was measured immediately after extubation (21.4 ± 2.7 hours). Fifteen patients had smoked within the past year, but none had a history of pulmonary impairment. Twenty-two patients had internal mammary artery (IMA) dissection. Operation and recovery were uneventful in all cases. After extubation, peak expiratory flow rate was decreased by 65%. At discharge, lung volumes were decreased by 19% to 33% below preoperative values and expiratory flow rates were decreased by 33% to 37% below preoperative values. Some minor changes were detected at 3 months. Further analysis of these changes according to smoking history, age, preoperative weight, dissection of IMA, and aortic cross-clamp time showed that only IMA dissection affected the postextubation changes in peak expiratory flow rate ($p < 0.0001$), whereas the decreases in functional residual capacity and expiratory reserve volume at discharge were affected by IMA dissection ($p < 0.05$) and age ($p = 0.01$). Thus, median sternotomy is associated with severe but short-term pulmonary dysfunction; IMA dissection has a significant adverse effect on these changes.

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Median sternotomy has become the usual approach in cardiac surgery because of the excellent exposure obtained and the reduced morbidity achieved as compared with lateral thoracotomy [1]. Several older studies indicated better and earlier preservation of pulmonary function with median sternotomy [1–3], whereas others reported no differences between the two techniques [4, 5]. A careful evaluation of pulmonary function both before and after coronary artery operations published by Braun and colleagues [6] demonstrated a significant reduction in lung volumes, diffusion capacity, and oxygenation 2 weeks after operation, with partial improvement 4 months later. Their data were obtained no earlier than 2 weeks after operation, however, and did not include an evaluation of expiratory flow rates. Furthermore, recent improvements in both intraoperative and postoperative care might affect these previously observed changes in pulmonary function.

The purpose of this study was to determine the effect of median sternotomy during coronary revascularization on both early and late pulmonary function. We also sought to identify factors that may affect these changes.

Material and Methods

Twenty-nine consecutive male patients undergoing elective coronary artery revascularization were studied. The mean age was 56 ± 5.1 years (range, 42 to 71 years); 12 patients were aged 60 years or more. Fifteen patients had smoked (70 ± 42 pack-years) during the past year ("smokers"). Of the remaining 14 ("nonsmokers"), 6 did not smoke during the previous 10 years and 8 stopped smoking between 1 and 10 years before operation. No subject had a past medical history or physical examination consistent with lung disease. Five patients had an anterior-apical left ventricular aneurysm. Each subject answered a questionnaire on respiratory symptoms. No subject had obstructive lung disease as defined by a preoperative $FEV_1/FVC\%$ less than 0.69 (FEV_1 = forced expiratory volume at 1 second; FVC% = percentage of forced vital capacity). Percentage deviation of perioperative body weight from ideal weight [7] was calculated for each patient. The mean deviation for the entire group was 21.8% ± 14.6% (range, −4.5% to +56.4%). Fifty-eight percent of the patients were 20% or more above their ideal weight. The protocol was approved by the institutional committee for human studies.

All subjects underwent complete pulmonary function tests. Lung volumes (slow vital capacity, residual volume, inspiratory capacity, functional residual capacity [FRC], expiratory reserve volume [ERV], and total lung capacity), expiratory flow rates (forced vital capacity [FVC], FEV_1,

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$FEV_1/FVC\%$, $FEV_3/FVC\%$, forced expiratory flow between 25% and 75% of FVC [FEF25–75%], and peak expiratory flow rate [PEFR]), diffusion capacity (DLCO), and arterial blood gases were measured. All studies were performed 1 day before operation, before discharge (average 8.7 ± 1.9 days), and at 3 months postoperatively. Peak expiratory flow rate was also determined immediately after extubation. Static lung volumes were calculated using the closed-circuit helium dilution technique. Forced expiratory flow rates were measured using a Mediscience Wedge Spirometer (Pulmonizer 525, Medsciences, Needham Heights, attached to a Hewlett-Packard X-Y plotter [7041A]). Peak expiratory flow rate was measured with a Wright peak flow meter, and DLCO was determined by the single breath method [9]. Predicted values for pulmonary function tests were calculated from regression equations according to age, height, and sex [9, 10]. Arterial blood gases, serum hemoglobin, and carboxyhemoglobin were also measured using a blood gas analyzer and cooximeter (Instrumentation Laboratories 813 blood gas analyzer with 282 cooximeter for hemoglobin, oxygen saturation, and carboxyhemoglobin).

The surgical approach was through a median sternotomy incision, and dissection of the left internal mammary artery (IMA) was performed from its origin to the seventh rib and was facilitated by use of a Favaloro retractor. A left ventricular aneurysm was plicated or resected in 5 patients. The sternum was reapproximated by placement of three No. 5 figure-of-8 wire sutures. All patients were extubated the morning of the first postoperative day (21.4 ± 2.7 hours after operation).

Statistical Analysis

Statistical analysis was made in three stages. First, baseline values (preoperative) were compared by a paired *t* test with predicted values for each pulmonary function variable.

Second, using the ratio of each patient's pulmonary function variable to the predicted value, changes over time (preoperative to after extubation, to discharge, and to 3-month follow-up appointment) were assessed using a two-factor analysis of variance for a repeated-measures design (factors are patient and time). When significant changes over time were identified, Tukey's test was used to determine which time points were different.

Third, when significant differences were identified over time (steps 1, 2), regression analysis was used to determine which of five independent variables (age, smoking history during the year before operation, percentage deviation of preoperative weight from ideal weight, IMA dissection, and perfusion time) affected the changes from baseline over time. For this analysis, the dependent variable was the difference between the ratio of the pulmonary function variable at a particular time to predicted value and the ratio of the baseline value to the predicted value. Each of the independent variables was examined separately, followed by multiple regression analyses with combinations of two, three, and five independent variables to determine the effect of one independent variable while adjusting for the others. The two-, three-, and five-variable regressions gave very similar results. The intermediate two- and three-variable regressions were performed because of concern over the small sample size ($n = 29$) for a five-variable regression. In all these regressions, the baseline ratio was included as an independent variable to adjust for possible effect of baseline values on changes over time.

A significance level of 0.05 was used for all statistical testing.

Results

There were no serious postoperative pulmonary complications, but most patients (25/29) had postoperative radiological findings suggesting either segmental or subsegmental atelectasis, which was treated routinely with chest physiotherapy. This finding was still present in 16 patients at discharge (14 of them were smokers). These changes were insignificant clinically and by 3 months had resolved in all patients. None of the patients had postoperative phrenic nerve injury or hemothorax.

The mean aortic cross-clamp and pump times were 67 ± 28 (range, 11 to 143) and 120 ± 43 (range, 32 to 233) minutes, respectively. Nine patients received between 2 and 6 U of blood transfused through a fine filter (Shiley arterial 20-μm filter). Twenty patients did not require any type of blood product transfusion. The number of distal anastomoses per patient was 4.4 ± 1.8 (range, two to seven). The left IMA was used in 22 patients. The IMA was not used when its free flow was less than 50 mL/min or when the left anterior descending, diagonal, or proximal circumflex marginal coronary arteries did not require bypass. The pleural space was opened in 13 patients in association with the left IMA graft dissection. A chest tube was placed in the pleural space of 7 patients.

Mean preoperative, predicted, and postoperative values for lung volumes, expiratory flow rates, diffusion capacity, and arterial blood gases for the entire group ($n = 29$) are shown in Table 1. Comparison between preoperative and predicted values is shown in Table 2. Preoperatively, FVC, FEV_1, FEF25–75%, and DLCO were significantly lower than predicted values. At discharge, with the exception of residual volume, all volumes were reduced by 19% to 33% below preoperative values. At 3 months, all volumes returned to preoperative values, except the inspiratory capacity, which was slightly lower than the preoperative value. At periextubation time, PEFR was reduced to 35% of its preoperative value. At discharge, all expiratory flow rates except FEV_3/FVC were decreased by as much as 37%. At 3 months, except for FVC and FEV_1, which remained statistically lower, all expiratory flow rates returned to baseline.

The diffusing capacity, which was significantly lower than the predicted values preoperatively, was significantly higher than its preoperative value at 3 months. After extubation, arterial oxygen and carbon dioxide tensions were significantly elevated (mean inspired O_2 concentration, 46.2% + 7.2%). At discharge, both arterial oxygen and carbon dioxide tensions were significa lower than the preoperative values measured on

Table 1. Effect of Midsternotomy on Postoperative Pulmonary Function and Blood Gas[a]

Variable	Preoperative	Predicted	Postextubation	Discharge	3 mo
Lung volumes					
SVC (L)^d	4.1 ± 0.16	4.2 ± 0.13	. . .	2.8 ± 0.16^e	3.9 ± 0.16
RV (L)	2.4 ± 0.15	2.2 ± 0.04	. . .	2.2 ± 0.16	2.5 ± 0.12
IC (L)^d	3.2 ± 0.11	3.1 ± 0.1	. . .	2.2 ± 0.15^e	2.9 ± 0.1^e
FRC (L)^b	3.3 ± 0.17	3.4 ± 0.08	. . .	2.7 ± 0.2^e	3.6 ± 0.21
ERV (L)^b	0.89 ± 0.08	1.2 ± 0.09	. . .	0.68 ± 0.08^e	0.99 ± 0.1
TLC (L)^d	6.6 ± 0.2	6.3 ± 0.18	. . .	5.0 ± 0.21^e	6.0 ± 0.2
Lung airflow rates					
FVC (L/s)^d	4.0 ± 0.15	4.2 ± 0.13	. . .	2.7 ± 0.10^e	3.7 ± 0.14^e
FEV_1 (L/s)^d	3.1 ± 0.11	3.3 ± 0.11	. . .	2.1 ± 0.13^e	2.9 ± 0.12^e
FEV_1/FVC%^{c}	80.0 ± 1.24	80.6 ± 0.24	. . .	77.6 ± 1.4^e	78.8 ± 1.1
FEV_3/FVC%	95.6 ± 0.52	97.0 ± 0	. . .	94.9 ± 0.64	95.2 ± 0.75
FEF25–75%^{d}	3.2 ± 0.16	4.2 ± 0.11	. . .	2.0 ± 0.18^e	2.8 ± 0.16^e
PEFR (L/s)^d	8.2 ± 0.37	8.4 ± 0.19	2.9 ± 0.40^e	5.7 ± 0.40^e	7.8 ± 0.40
DLCO (mL/min/mm Hg)^d	22.3 ± 1.0	24.6 ± 1.2	. . .	20.1 ± 1.4	26.4 ± 1.1^e
PaO_2 (mm Hg)^b	80.7 ± 1.4	. . .	103 ± 5.0^{e,f}	72.2 ± 2.0^e	85.7 ± 1.7
O_2 saturation (%)	95.4 ± 0.31	. . .	96.4 ± 0.30	94.3 ± 0.44	95.1 ± 0.51
$PaCO_2$ (mm Hg)^b	37.0 ± 0.8	. . .	40.2 ± 1.0	31.9 ± 0.8^e	36.0 ± 0.7
Serum hemoglobin (mg/L)^c	137 ± 3.7	. . .	87 ± 3.0^e	96 ± 3.1^e	135 ± 2.8
Body weight^b	83.7 ± 2.4	. . .	86.0 ± 2.4^e	82.4 ± 2.4	80.1 ± 2.3^e

[a] Values are shown as mean ± standard error of the mean. [b] $p = 0.05–0.01$, [c] $p = 0.01–0.001$, [d] $p < 0.001$: denotes variables that have changed significantly over time (repeated-measures analysis of variance). [e] Point at which significant differences ($p < 0.05$) in time occurred (Tukey multiple comparison). The ratios of the values at each time point to predicted values were used for this analysis. Therefore, comparisons between preoperative and predicted values are not included in this table. For comparisons between preoperative and predicted values, see Table 2. [f] Fractional concentration of inspired oxygen = 46.2% ± 7.2%.

DLCO = diffusing capacity; ERV = expiratory reserve volume; FEF25–75% = forced expiratory flow between 25% and 75% of FVC; FEV_1 = forced expiratory volume in first second; FRC = functional respiratory capacity; FVC = forced vital capacity; IC = inspiratory capacity; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension; PEFR = peak expiratory flow rate; RV = residual volume; SVC = slow vital capacity; TLC = total lung capacity.

whereas at 3 months arterial oxygen tension was significantly improved. Mean hemoglobin level, which had been 137 ± 20 g/L (13.7 ± 2.0 g/dL) at admission, decreased after operation to 87 ± 16 g/L (8.7 ± 1.6 g/dL) after extubation. It was still lower than preoperative values at discharge and returned to the preoperative level at 3 months. On admission, carboxyhemoglobin ranged between 0.7% and 6.8% (mean, 2.0% ± 1.5%) of total hemoglobin. Mean body weight increased significantly from 83.7 ± 2.4 to 86.0 ± 2.4 kg at periextubation but at discharge was not significantly different from the postoperative value.

The effect of the three preoperative independent variables (age, smoking history, and weight) on the difference between preoperative and predicted values is shown in Table 2. Age affected DLCO, weight affected FVC and

Table 2. Comparison Between Preoperative and Predicted Values of Pulmonary Function Variables

		Effect of Independent Variables on Differences Between Predicted and Baseline Values			
		Univariate Analysis			
Variable	Overall (Paired t Test)	Age	Smoking History	Weight	Multiple-Regression Analysis
FRC	NS	NS	$p = 0.1$ (NS)	NS	Smoking, $p = 0.07$
FVC	$p < 0.05$	NS	NS	$p < 0.05$	Weight, $p = 0.07$
FEV_1	$p < 0.05$	NS	NS	$p < 0.05$	Age, $p < 0.05$[a]
FEF25–75%	$p < 0.001$	NS	NS	NS	. . .
DLCO	$p < 0.05$	$p < 0.05$ (+)	$p = 0.1$ (NS)	NS	. . .

[a] Positive relationship between DLCO and age. All other relationships between pulmonary function variables and independent variables were negative.

NS = not significant, other abbreviations as in Table 1.

Table 3. Relationship Between Independent Variables and Postoperative Changes in Pulmonary Function

	Univariate Analysis					
Variable	Age	Smoking History	Weight	IMA	Pump Time	Multiple-Regression Analysis
SVC	NS	NS	NS	NS	NS	NS
IC	NS	NS	NS	NS	NS	NS
FRC	NS	Discharge $p = 0.1$ (NS), 3 mo $p < 0.05$	NS	NS	NS	IMA at discharge $p < 0.05$, age at discharge $p = 0.01$, smoking history at 3 mo $p = 0.05$
ERV	NS	Discharge $p = 0.1$ (NS), 3 mo $p < 0.05$	NS	NS	NS	IMA at discharge $p < 0.05$, age at discharge $p = 0.01$, smoking history at 3 mo, $p = 0.05$
TLC	NS	NS	NS	NS	NS	NS
FVC	NS	3 mo $p = 0.05$	NS	NS	NS	Smoking history at 3 mo $p = 0.05$
FEV_1	NS	Discharge $p = 0.09$ (NS)	NS	NS	NS	NS
FEV_1/FVC%	NS	NS	NS	NS	NS	NS
FEF25–75%	NS	NS	NS	NS	NS	NS
PEFR	NS	NS	NS	Postextubation $p < 0.0001$	NS	IMA at extubation $p < 0.0001$
DLCO	NS	NS	NS	NS	NS	NS

IMA = internal mammary artery; other abbreviations as in Table 1.

FEV_1, and smoking history probably affected FRC and DLCO. Multiple regression analysis using the three independent variables indicate that the effect of age on DLCO, of weight on FEV_1, and probably of smoking history on FRC were independent of the other variables in their effect on the difference from baseline. Only the relationship between age and DLCO was positive. All other relationships between pulmonary functions and independent variables were negative.

Examinations of the effect of each of the five independent variables on the postoperative changes in pulmonary function (Table 3) indicate that none affected the changes in slow vital capacity, inspiratory capacity, total lung capacity, FEV_1/FVC, FEF 25–75%, and DLCO. The changes in PEFR were affected after extubation by IMA dissection (Fig 1). After adjustment for the remaining four independent variables and for differences in baseline by multiple regression analysis, IMA dissection remained the only independent variable that significantly affected changes in pulmonary function at postextubation. The changes in PEFR in patients in whom IMA dissection was associated with opening of the left pleural space (n = 13) were not different from the changes in patients with intact left pleura (n = 9). Smoking history showed a borderline significant effect on FRC, ERV, and FEV_1 at discharge by univariate analysis. Use of this analysis showed that age and IMA dissection were not significant independent variables affecting FRC and ERV, but after adjustment was made for the remaining independent variables by multiple-regression analysis, age and IMA dissection were shown to affect FRC and ERV significantly at discharge. None of the other variables showed a significant effect on the changes in pulmonary function by multiple-regression analysis postextubation and at discharge.

Comment

A complete evaluation of the preoperative and postoperative pulmonary function was performed in a group of 29 unselected male patients undergoing coronary artery revascularization. We believe that this group represents the

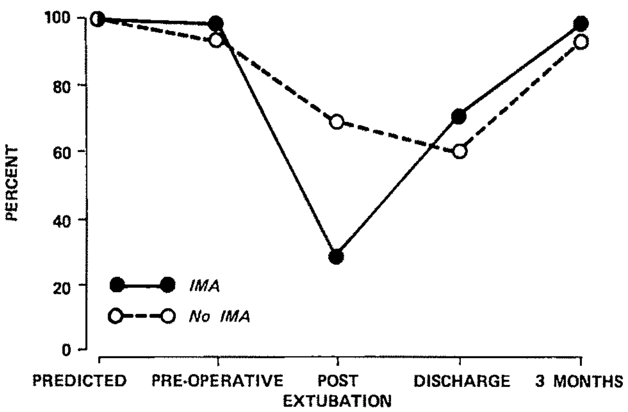

Fig 1. Plot of peak expiratory flow rate over time for patients who underwent internal mammary artery (IMA) dissection and for patients who did not undergo IMA dissection. Values are presented as ratios to predicted values. The groups at postextubation were significantly different (p < 0.001) by multiple regression analysis after adjustment was made for age, weight, perfusion time, smoking history, and baseline peak expiratory flow rate.

US male population with coronary artery disease who undergo bypass grafting.

When the entire group was analyzed, minor but statistically significant preoperative reductions in FVC, FEV_1, and FEF 25–75% were observed, which may represent early chronic obstructive lung disease [11]. Postoperatively, a restrictive pulmonary pattern affecting all lung volumes was observed. Proportional reductions in lung airflow rates observed in these patients are expected to occur in association with a decrease in vital capacity and do not indicate a concomitant obstructive pattern. Most lung volumes and air flow rates were between two thirds and three quarters of preoperative values at discharge, whereas only minor changes were measured at 3 months. The PEFR could be measured immediately after extubation and was as low as 35% of the preoperative value. The residual volume remained unchanged, which suggests that no significant gas trapping from peribronchial fluid accumulation after operation was noted. The finding of hypoxemia disclosed ventilation–perfusion mismatch, which is a frequent finding in the immediate postoperative period [12]. Clinically significant hypoxemia was not present in our patients at discharge or at 3 months, however.

Coronary artery bypass grafting is associated with several interventions that may alter pulmonary function. Among these are median sternotomy, establishment of extracorporeal circulation, deflating of the lungs during the ischemic period, transfusion of blood, and in certain patients, the freeing up of the IMA pedicle by dissection from the chest wall. These interventions may result in chest wall pain, tenderness and stiffness, and increased extravascular lung water [13], as well as increased production and accumulation of secretions in the tracheobronchial tree [14].

Previous reports [4, 6, 15–18] have indicated significant and prolonged (4 months) impairment in pulmonary function after open heart operations. Our data showed less and only transient impairment, which may reflect improvements such as those in extracorporeal circulation technology and in perioperative pulmonary managements and the infrequent transfusion of blood products used in current management of patients.

To determine what may have influenced these changes in pulmonary function, the effects of smoking in the past year, IMA dissection, age, percentage deviation of preoperative weight from ideal weight, and pump time were evaluated. The better diffusion capacity among the older population preoperatively resulted from the fact that most of the younger patients were smokers (76% smokers among patients aged less than 60 years, 16% smokers among patients aged more than 60 years) [19, 20]. The DLCO improved at 3 months to a level significantly higher than the preoperative value and similar to the predicted value, probably because patients ceased smoking.

By univariate analysis, the PEFR after extubation was shown to be affected by IMA dissection, and FRC, ERV, and FEV_1 at discharge to be probably affected by smoking history. Even after adjustment was made for the remaining independent variables and for differences in baseline by multiple-regression analysis, dissection of the IMA was still an independent variable associated with significant impairment of postoperative pulmonary function. Specifically, IMA dissection adversely affected the PEFR after extubation and ERV and FRC at discharge. The PEFR, the only bedside test that could be obtained immediately after extubation, had decreased to as low as 35% of its preoperative value among patients with IMA dissection and improved to 70% at discharge. The airflow rates generated at maximum expiratory force are directly related to the chest wall elastic recoil and the force of the expiratory muscles [21]. This correlates with the ability to cough effectively and with the incidence of postoperative respiratory complications [22]. The impairment in PEFR resulted from weakening of expiratory muscles and chest wall pain, edema, and stiffness incurred by the IMA dissection and retractor pressure to the cartilages and ribs. The reduction of FRC, a function that reflects the balance between the tendency of the thoracic cage to expand and the elastic recoil of the lungs [23], indicates that pain and decreased compliance due to IMA dissection was still present at discharge. This may be associated with atelectasis and ventilation-perfusion mismatch [24]. Previous reports [25, 26] have described adverse effects in pulmonary function in patients with pleurotomy. Pleurotomy in our study did not modify pulmonary function further.

Although considered to be relatively benign, median sternotomy was shown to be associated with a rather severe but short-term pulmonary dysfunction; IMA dissection was the most significant variable that affected these changes. Although of no consequence in a population free of lung disease, in patients with a preoperative compromised or marginal pulmonary reserve owing to preexisting obstructive or restrictive lung disease, postoperative impairment in pulmonary function may result in serious complications. In such patients, preoperative pulmonary function testing followed by vigorous chest physiotherapy, minimizing chest wall traction and trauma to ribs and soft tissue during IMA dissection, or even complete avoidance of IMA use may decrease the risk of pulmonary complications after median sternotomy.

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Excision of the Aortic Wall in the Surgical Treatment of Acute Type-A Aortic Dissection

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Between March 1986 and September 1988, 38 patients underwent extended aortic resection (aortic valve, ascending aorta, and arch) for acute type-A aortic dissection with aortic valve insufficiency; deep hypothermia and circulatory arrest were used. All patients were operated on within 17 hours of the onset of symptoms. In the first 24 patients, operation was performed by the "inclusion technique." In the last 14 patients, the "excision technique" was used: the ascending aorta and arch was excised, and the aorta was transected at the beginning of the descending thoracic tract. Excision and transection were considered essential to prevent back flow from the false lumen, which is the main source of bleeding, and to allow all anastomoses to be constructed beyond the limits of dissection. The only anastomosis to the dissected aorta was at the distal end of the graft. One of the 14 patients died (7.1%). One patient was reopened for bleeding: blood was issuing from the attachment of the carotid trunks, and the defect was repaired by interposing a bifurcated Dacron graft between the arch graft and the carotid arteries. Extended aortic excision meets the principle of either eliminating as far as possible the diseased aorta or controlling intraoperative and postoperative bleeding. An operation of great magnitude can be considered a life-saving procedure when compared with the high risk of acute type-A aortic dissection.

(Ann Thorac Surg 1990;50:274–6)

Acute aortic dissection needs to be defined: what should constitute acute dissection? We believe that dissection is acute in the first hours of onset of symptoms; conversely, many investigators believe that a dissection lasting 15 days is acute. At 15 days, some patients are dead. Many deaths occur in the first hours after onset of symptoms, with an attrition rate of 1 patient per hour [1]; furthermore, a 15-day dissection does not pose technical problems as great as those of a dissection in the first hours. We believe that type A dissection should be treated as soon as possible. The major threat of these emergency operations is bleeding, which comes from the anastomoses between graft and dissected aorta where the false lumen very rarely can be closed. We therefore made efforts to resect the dissected aorta extensively to have a better chance to obliterate dissection and to perform bloodless anastomoses. In a previous article [2], we reported 24 patients treated with extended aortic resection and "inclusion technique." Later, we introduced the concept of excising the dissected aorta to perform all the anastomoses beyond the limits of dissection: the aortic valve was excised together with the ascending aorta and arch, and the aorta was transected at the beginning of the descending thoracic tract, thus confining dissection to the distal part [3]. This article describes the latter technique and reports our first results.

Material and Methods

Patients

From March 1986 through September 1988, 14 patients (11 men and 3 women) were operated on with the "aortic excision technique" for acute type-A aortic dissection (13 had aortic valve insufficiency). The patients ranged in age from 49 to 85 years (mean age, 56 years); all of them had anterior retrosternal pain with transient cardiocirculatory collapse in 9 and prolonged hypotension in 2 patients with pericardial tamponade. Five patients had transient neurological signs. Three patients had undergone previous cardiac operations: 2 had aortic valve replacement for aortic valvar insufficiency and 1 had coronary bypass.

Operation was started within 5 hours of admission and 10 hours of onset of symptoms. While the operating room was being prepared, angiography was performed in all patients.

Surgical Technique

Aortic excision was performed through median sternotomy, and a valved conduit graft sufficed to replace the resected aorta. Extracorporeal circulation was instituted with the arterial return cannula in a femoral artery and a single venous cannula into the right atrium; the left side of the heart was vented through the right superior pulmo-

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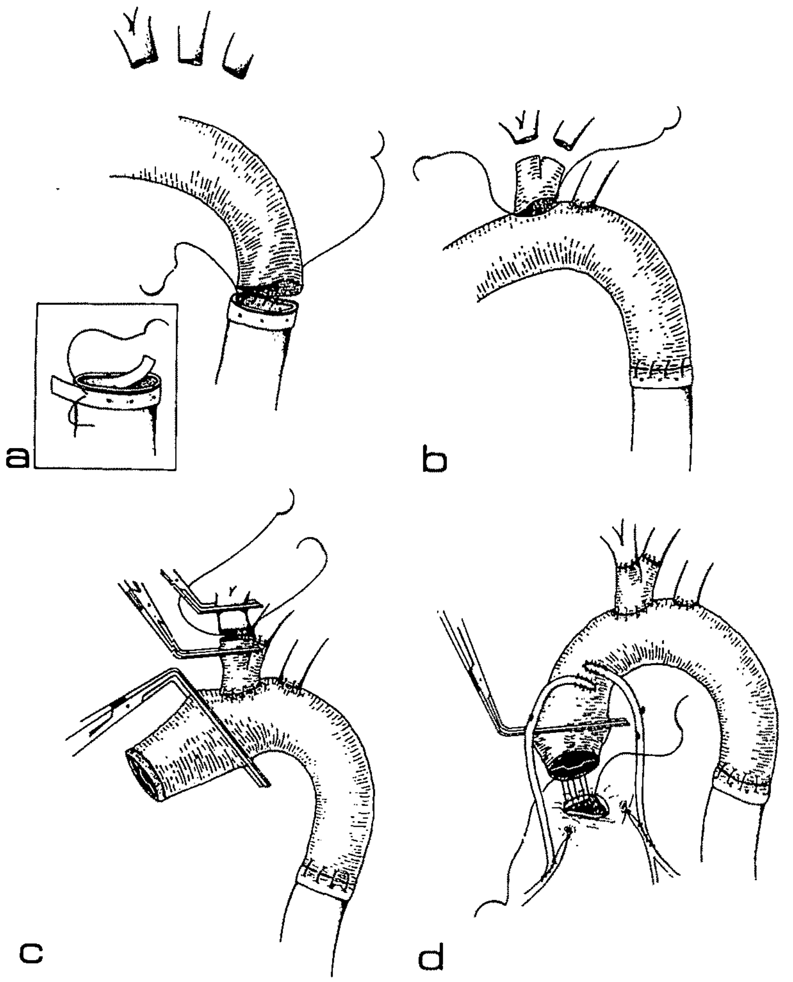

Fig 1. Aortic arch replacement. (a) The distal end of a composite valve graft is anastomosed to the descending thoracic aorta where dissection has already been closed. (b) The carotid arteries are anastomosed to the arch graft by interposition of a bifurcated Dacron graft to reach the limit of dissection. (c) The arch graft is cross-clamped, and extracorporeal circulation and rewarming are started. (d) After the coronary attachment is complete, the clamp is moved distally and the valve is sutured to the annulus.

nary vein. When cannulation was complete, core cooling was started, the ascending aorta was cross-clamped, and hypothermic cardioplegia was injected. The aorta was opened, the aortic root was inspected, and the aortic valve was removed. At the same time, both coronary arteries were ligated at their origin from the aortic wall [4] and were connected, beyond the limits of dissection, with the distal end of two vein grafts (Fig 1d).

At a core temperature of 14°C, cardiopulmonary bypass was discontinued with the patient in head-down position, the carotid arteries were clamped, and the arteriovenous lines were occluded. The aortic incision was extended into the arch to locate the carotid orifices; the ascending aorta and arch were then excised, and the aorta was transected at the beginning of the descending tract. Dissection was closed at the mouth of the distal aorta with interrupted stitches on circular Teflon collars (Fig 1a). Arch replacement was started by anastomosing the distal end of a composite valve graft to the descending thoracic aorta (Fig 1a); the carotid arteries were then connected to the graft as well (Fig 1b). Subsequently, the arch graft was cross-clamped at the preinnominate area (Fig 1c) and cardiopulmonary bypass with rewarming was resumed. During rewarming, both venous coronary bypass grafts were attached to the graft and, finally, the valved end of the graft was sewn to the aortic annulus, with coronary perfusion already started (Fig 1d).

With this procedure, body temperature was lowered to 14°C and the time of circulatory arrest averaged 40 minutes. The carotid arteries were attached to the graft by different techniques: a button of aortic wall was used in 4 patients, a bifurcated Dacron graft (16 mm) was interposed in 8 patients, and both branches of the interposed graft were anastomosed to the carotid arteries in the neck in 2 patients [3].

Results

One of 14 patients died (7.1%) of respiratory insufficiency due to excessive manipulation of the left lung. One patient was reopened on the second postoperative day because of bleeding from the anastomosis of the carotid trunks, which had been fashioned according to the button technique. The defect was repaired by suturing a bifurcated Dacron graft (16 mm) to the arch graft and reconnecting the carotid arteries one at a time without extracorporeal circulation. The patient recovered after 7 days of renal dialysis.

Follow-up averaging 30 months (range, 15 to 45 months) was available in all patients. No late complications occurred. Ten patients are in functional class II and 4 are in class III.

Comment

Aortic excision is an operation of great magnitude, but it is in proportion to the very high risk of acute type-A aortic dissection. We support the principle of an emergency operation with extended excision and transection of the aorta to interrupt back flow from the false lumen that is the main source of bleeding at the anastomoses. All anastomoses of the arch are at high risk of bleeding if not constructed beyond the limits of dissection; according to the aortic excision technique, the only anastomosis with the dissected aorta is at the distal end of the graft. At this level, dissection is always concentric and can be easily closed, allowing a safe anastomosis with the graft. The only perioperative bleeding occurred in a patient in whom the connection with the arch vessels had not been performed beyond the limits of dissection.

The graft inclusion technique, previously described [2], was not always effective in obliterating dissection; thus, some patients died of persistence of ostial stenoses in the abdominal visceral arteries. Other investigators [5, 6] reported a hematoma around the graft in the ascending aorta that had to be decompressed. Because of these potential defects, we abandoned graft inclusion in favor of aortic excision.

Acute type-A aortic dissection with aortic valvar insufficiency is a life-threatening disease requiring emergency treatment. We believe that as a life-saving procedure even an extended aortic resection should be considered. Although the small number of cases does not allow us to draw conclusions, we believe that excision and grafting of the diseased aorta beyond the limits of dissection should be the treatment of choice.

Addendum

From September 1988 to December 1989, 3 additional cases of acute type-A aortic dissection were operated on using the excision technique. The patients were all men, aged 52, 69, and 70 years. The duration of the dissection averaged 12 hours. One patient had left hemiparesis at the onset of symptoms but later recovered. All patients underwent angiography, and aortic valvar insufficiency was present in each. Operation was performed using the described technique; in each case the carotid arteries were reconnected with graft interposition. The last patient to undergo the procedure had neurological signs postoperatively thought due to gaseous emboli but recovered completely after 1 week. No early or late death was registered, bringing our mortality rate to 5.9% (1/17). Five, 6, and 11 months after all operations, patients are asymptomatic and leading normal lives.

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Decreased Vascular Compliance After Reimplantation of the Left Lower Lobe in Young Pigs

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The effects of chronic denervation on pulmonary vasculature are not well understood. Three groups of young pigs were prepared: (1) those receiving sham thoracotomy, (2) those having left upper lobectomy alone (innervated left lower lobe), and (3) those receiving left pneumonectomy followed by reimplantation of the left lower lobe (denervated left lower lobe). At 10 weeks after operation, animals were anesthetized and instrumented for study. No changes in baseline pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output, or pulmonary vascular resistance were observed. With diversion of the entire cardiac output to the left lung or lobe, however, the group with reimplanted lobes had a significantly higher pulmonary artery pressure and pulmonary vascular resistance than the other groups. This may result from chronic denervation of the pulmonary vasculature and receptor upregulation.

(Ann Thorac Surg 1990;50:277–80)

The advent of cyclosporine for the treatment of rejection [1] and the technical advance consisting of wrapping the bronchus with omentum [2] have allowed, for the first time, reliable bronchial anastomotic healing. These advances together ushered in a modern era of heart-lung and lung transplantation, and the landmark work of the Toronto Transplant Group made isolated lung transplantation a clinical reality in humans [3]. Unfortunately, as patients (and experimental models) survive transplantation into the medium term, conditions such as obliterative bronchiolitis and pulmonary superinfection arise, limiting long-term survival for heart-lung transplantation [4]. Modification of variables such as immunosuppression and surgical technique will undoubtedly help to minimize these midterm problems. Other less manipulatable variables also have substantial impact. Hilar denervation clearly is unavoidable, and its physiological effects are incompletely understood. We previously reported a loss of dynamic airway compliance in reimplanted lobar segments as assessed in the chronic state [5]. We believe that this represents chronic bronchial constriction due to denervation, based in large part on the absence of anatomically demonstrable fixed airway obstruction [5].

Previous research has demonstrated that the lung is invested with both sympathetic and parasympathetic fibers, with the latter predominating [6]. Stimulation of sympathetic outflow to the lungs results in a decrease in compliance in large elastic arteries, reflected in an increased pulmonary vascular resistance and pulmonary artery pressure only under high-flow conditions (increased cardiac output) [6]. Acute sympathectomy produces vasodilatation, suggesting a tonic vasoconstrictive influence on the pulmonary arterial bed [7–9]. The purpose of the present study was to determine the effects of chronic denervation in the pulmonary vascular bed.

Material and Methods

At approximately 10 weeks of age (mean age, 10 ± 1 weeks), 14 young pigs underwent left thoracotomy and left lung manipulation. Three study groups were defined. Group 1 consisted of 4 animals who underwent sham thoracotomy alone. Group 2 (5 animals) underwent left upper lobectomy and therefore maintained an innervated left lower lobe. Group 3 consisted of 5 animals subjected to left pneumonectomy and reimplantation of the left lower lobe, which resulted in a denervated lobe. The procedure used for group 3 consisted first of pneumonectomy performed distal to vascular clamps on the proximal left main pulmonary artery (PA), on the proximal left main bronchus, and isolating the left atrial origin of the pulmonary veins (Fig 1). The left lung was perfused at 5°C with Ringers' lactate until a clear effluent from the pulmonary veins was seen. A left lower lobe dissection was then performed, preserving the full length of the PA, bronchus, and the inferior pulmonary veins. The lower lobe was immersed for approximately 5 minutes in iced Ringers' lactate before reimplantation. An anastomosis was performed from the inferior pulmonary vein to the left atrium, the bronchus was then reunited, and finally the PA was anastomosed. The vascular anastomoses were performed with running 6-0 absorbable monofilament suture, and the bronchial anastomosis was performed with running 4-0 monofilament absorbable suture. The

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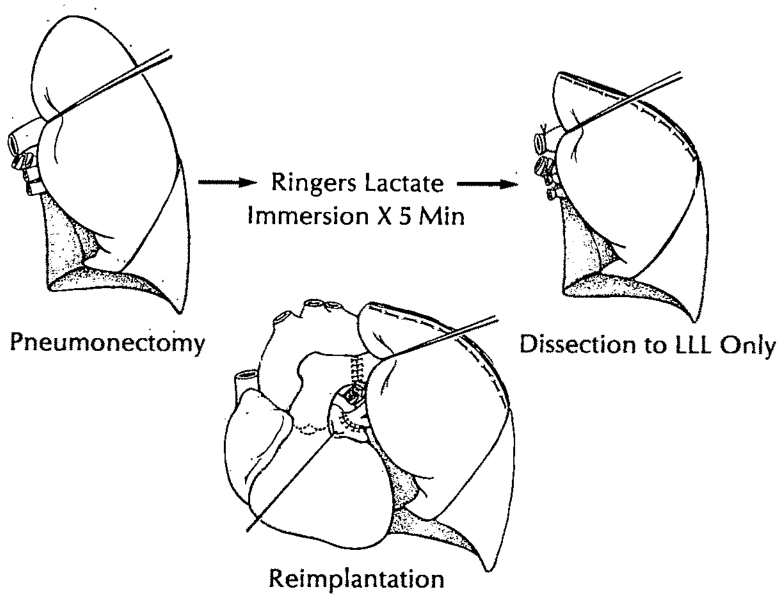

Fig 1. Surgical technique for left pneumonectomy and reimplantation of the left lower lobe (LLL).

bronchial anastomosis was then wrapped circumferentially with a pedicle of omentum brought through an incision in the left hemidiaphragm in the technique described by Morgan and colleagues [2]. The omentum was anchored at both the diaphragm and bronchus with interrupted silk sutures. A chest tube was then positioned and connected to suction, and the thorax was closed in layers.

All animals were allowed to recover for 10 weeks before further study. Chest roentgenograms showed normal lung aeration. A fourfold increase in somatic weight was demonstrated, with a mean weight at 10 weeks of 80 ± 4 kg. Anesthesia was induced with ketamine (20 mg/kg) and maintained with intermittent intravenous pentobarbital. Pulmonary artery catheters were then placed through a right external jugular venous cutdown (7F, No. 93-131H, American Edwards Laboratory, Santa Ana, CA). A median sternotomy was performed with the PA catheter confirmed by palpation to be in the main PA. Pulmonary hemodynamic measurements were obtained in the steady state (before clamping). Carotid artery, central venous, and PA pressures were measured continuously with a multichannel recorder (ES1000, Gould, Inc, Cleveland, OH). The hilum of the right lung was then clamped (Fig 2), and the animals were allowed to stabilize for an additional 10 minutes. Pulmonary hemodynamic measurements were then repeated. The animals were killed after completion of the measurements and examined. The left lower lobe sections in groups 2 and 3 were fixed and stained for measurements of capillary surface area (adjusted for dry weight) by computerized planimetry.

The pulmonary specimens were prepared by perfusion of the bronchus with 10% formalin at a pressure of 20 to 25 cm H_2O for 1 to 2 hours. During preparation of sections, the lungs or lobes were divided in parallel slices extending from the hilum to the periphery. Block sections of tissues were randomly selected from the peripheral slices. In every case, volumetric proportions in nonoverlapping fields (3,000 points) from each section were examined [10]. Computerized planimetry was performed on a video monitor with a manual cursor (Zeiss Ortho-Plan, Karl Zeiss, Inc, Thornwood, NY). Sections were stained with an antibody specific for muscle actin (B-4 actin antibody), and the area of smooth muscle was calculated [11].

Results are expressed as the ratio of the area occupied by smooth muscle to that of capillary surface area. Statistical analysis among groups was performed using analysis of variance with Duncan's multiple-range test for multiple comparisons using the Statistical Analysis System. Paired comparisons were performed using Student's t test. Significance was considered achieved when a p value less than or equal to 0.05 was obtained.

All research protocols were reviewed and approved by the Animal Research Committee of the University of Virginia. These protocols conform to the guidelines put forth in the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Results

The results of the pulmonary hemodynamic measurements are shown in Table 1. The values are expressed as mean ± standard error of the mean before and after occlusion of the right pulmonary hilum. No significant differences were demonstrable before hilar occlusion. After hilar occlusion, PA pressures and pulmonary vascular resistance increased significantly ($p < 0.05$). There were no demonstrable differences in arterial blood gas measurements after occlusion.

Morphological analysis showed no significant difference between the calculated capillary surface area of the reimplanted lobes (group 3, 312 ± 60 $\mu m^2/g \times 10^3$) and those left lower lobes remaining after upper lobectomy (group 2, 427 ± 35 $\mu m^2/g \times 10^3$). The ratio of smooth muscle/capillary surface area was also not significantly

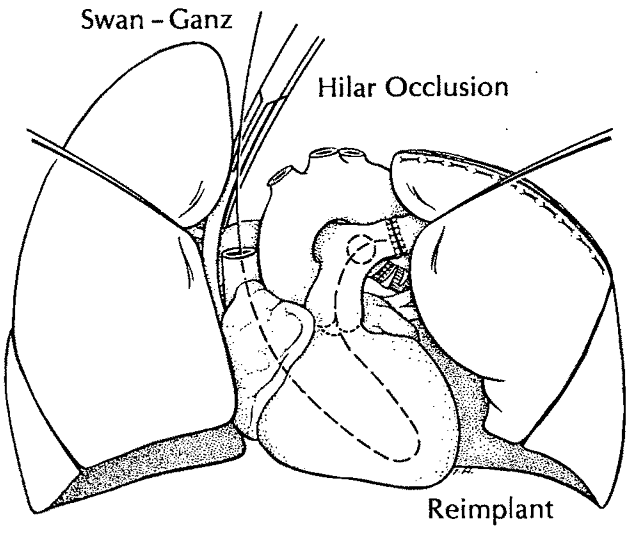

Fig 2. Instrumentation of animal at time of study 10 weeks after reimplantation.

different (group 2, 33 ± 3 × 10^{-2} versus group 3, 37 ± 2 × 10^{-2}).

Comment

Increases in flow in a healthy pulmonary vascular bed are accompanied by capillary recruitment, a resultant decrease in pulmonary vascular resistance, and maintenance of the pulmonary artery pressure [12]. Although this response appears to be preserved in animals undergoing thoracotomy alone or upper lobectomy alone, our results show a loss of compliance in the pulmonary vascular bed of the reimplanted lobe.

The etiology of the observed loss of vascular and airway compliance is unclear. Two main pathophysiological events are apparent: the ischemic and thermal insult the reimplanted lobe suffers and the complete hilar denervation that is produced. In this study, measurements of pulmonary vascular smooth muscle failed to demonstrate a fixed muscular obstruction in reimplanted lobes, and capillary surface area also appeared to have been preserved. Thus, diminution in pulmonary vascular capacitance due to injury seems unlikely to be the primary event.

The effects of denervation are less clear. Neither is it possible to rule out partial reinnervation after reimplantation. The pulmonary vasculature is well innervated with sympathetic and parasympathetic fibers [6]. The sympathetic outflow to the lung comprises both α-receptors (vasoconstriction) and β-receptors (vasodilatation), with the former predominating.

Thus, the net effect of sympathetic stimulation is vasoconstriction [4]. Surgical sympathectomy acutely produces vasodilatation, suggesting a tonic vasoconstrictive influence on the pulmonary bed [7, 8]. Parasympathetic stimulation of the lung, in contrast, produces vasodilatation [7], although parasympathectomy produces little change in the resting state [13]. Downing and Lee [6] noted that sympathetic fibers predominate in large elastic arteries of the lung. Stimulation of sympathetic outflow to the lung produced a decrease in compliance of these larger vessels, manifested as an increased pulmonary vascular resistance and PA pressure at higher cardiac outputs. This decrease in vascular compliance with sympathetic stimulation is similar to that observed in the animals in the present study.

Previous research demonstrated afferent stretch receptors in the main PA that trigger reflex efferent norepinephrine-mediated vasoconstriction in the pulmonary vascular bed [14]. At increased main PA volumes, the pulmonary capillary circulation is thus protected by reflex vasoconstriction, producing pulmonary hypertension. This is in contrast to the phenomenon of preservation of PA pressure through capillary recruitment observed within the range of normal autoregulation [12]. Humoral release of catecholamines, histamine, serotonins, or prostaglandins effects a complex interplay, but the various contributions of each are difficult to delineate [15]. The net effect of histamine or norepinephrine release is pulmonary vasoconstriction [15].

The reimplanted lobe is subject to the humoral stimulation of catecholamines and cholinergics, although denervation inhibits local release of neurotransmittors. The chronic effects of denervation may include up-regulation of receptors and increased sensitivity to humoral agents. The hypothesis that chronic denervation leads to an increased sensitivity to catecholamines and an augmented stress response warrants further investigation (Fig 3). We demonstrated normal hemodynamics in reimplanted lobes in the resting state. Increasing pulmonary blood

Table 1. Results of Pulmonary Hemodynamic Measurements[a]

	PA (mm Hg)		PCWP (mm Hg)		CO (L/min)		PVR (mm Hg/L/min)	
Group	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	22 ± 1	33 ± 8	8 ± 1	12 ± 2	7 ± 1	4 ± 1	1.8 ± 0.3	5.3 ± 1.4
2	24 ± 2	34 ± 2	11 ± 1	13 ± 2	5 ± 1	5 ± 1	2.8 ± 0.4	4.4 ± 0.5
3	23 ± 3	60 ± 13[b]	11 ± 2	21 ± 4	5 ± 1	4 ± 1	2.4 ± 0.4	12.7 ± 3.9[b]

[a] Results are shown as mean ± standard error of the mean. [b] $p \leq 0.05$ by analysis of variance.

CO = cardiac output; PA = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; Pre and Post = before and after occlusion of the right pulmonary hilum; PVR = pulmonary vascular resistance.

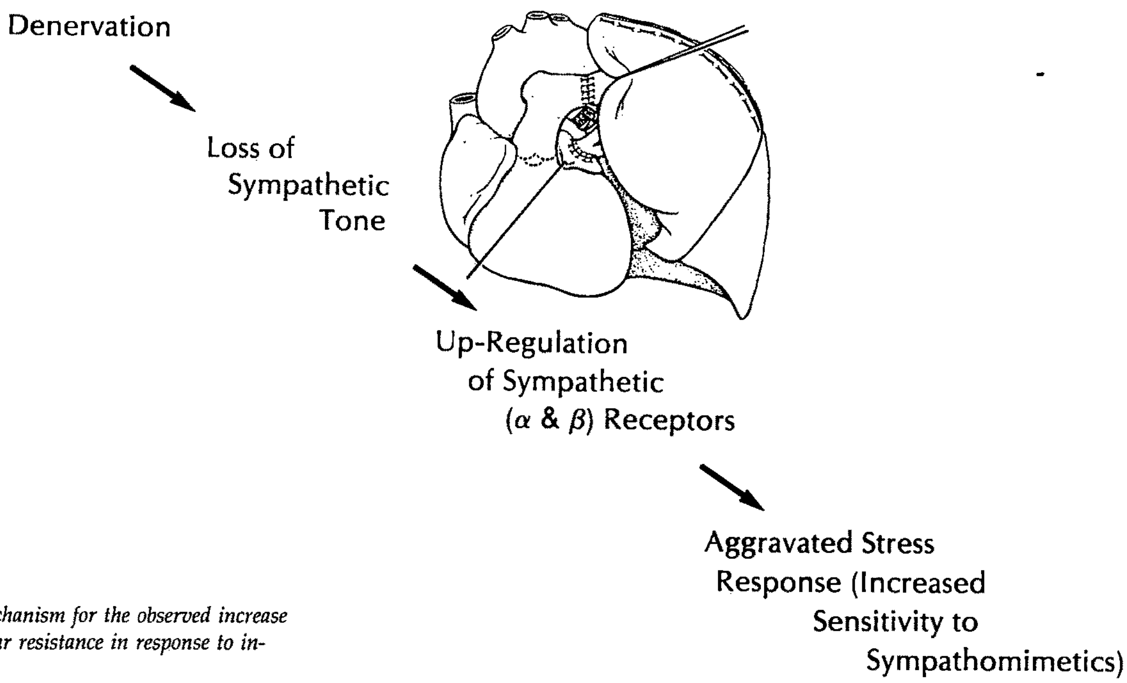
Denervation
Loss of Sympathetic Tone
Up-Regulation of Sympathetic (α & β) Receptors
Aggravated Stress Response (Increased Sensitivity to Sympathomimetics)

Fig 3. Presumed mechanism for the observed increase in pulmonary vascular resistance in response to increased blood flow.

flow, however, results in a marked increase in pulmonary vascular resistance. We believe that this augmented stress response is the result of chronic denervation, perhaps mediated by classic receptor up-regulation. This phenomenon should be present as well in clinical transplantation. Further investigation in this animal model and further clinical correlation in human transplants is required.

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Experimental Study of a New Porous Tracheal Prosthesis

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We studied the efficacy of a new tracheal prosthesis made of expanded polytetrafluorethylene reinforced with spiral silicone rings to repair circumferential tracheal defects in rabbits. Results showed an adequate consistency of prosthesis, adequate tolerance without producing tracheal stenoses, and impermeability to air, allowing a correct invasion by granulation tissue. This process was faster than any found in any other porous tracheal implant so far tested. We proved that epithelialization results from capillary invasion through the prosthetic pores and from growth from both tracheal ends. We conclude that this prosthetic material can be useful in repairing tracheal defects and may be the optimal tracheal graft for humans.

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Use of synthetic tubular grafts for correcting circumferential tracheal defects is always problematic, and many materials are used in accordance with existing knowledge and technology [1–13]. The existence of such a variety of grafts and surgical techniques leads us to believe that the ideal graft technique has yet to be discovered and that its identification is one of the current challenges in general thoracic surgery research.

When possible, the best surgical technique in tracheal reconstruction is resection and end-to-end anastomosis or autogenous tracheoplasty repair, but in some cases either pathology length, reduction in tissue elasticity in older patients, or fibrosis due to previous surgical procedures does not permit use of either technique. In such circumstances, a tracheal prosthesis may be necessary to reestablish air-passage continuity; this possibility has been described previously [14, 15].

We present the results of use of a new reinforced tracheal prosthesis with a smaller pore diameter than most used so far. According to our hypothesis, this should improve host tissue incorporation and consequently reduce complications.

Material and Methods

Ten albino Californian rabbits (*Oryctolagus cuniculus*) with an average weight of 3,150 ± 250 g and an average age of 152 ± 21 days were used. A porous tracheal prosthesis made of expanded polytetrafluorethylene (PTFE) reinforced with a continuous silicone spiral was implanted in the rabbits. The prosthesis used was Impraflex (Impra Sutures and Grafts, Paris, France) No. F7006 (6-mm inner diameter) because it is most similar to rabbit trachea. We implanted 4-cm long segments, which is approximately half the length of the trachea in these animals. Prostheses were sterilized in an autoclave with a regular cycle of 122°C for 30 minutes at 15 psi.

After 24 hours without food, the animals were immobilized and a cannula was introduced into the marginal vein of the ear. Anesthesia was induced with an intramuscular injection of ketamine hydrochloride (Ketolar), 25 mg/kg body weight, and was maintained with sodium pentobarbital, 20 mg/kg body weight, intravenously. Animals received an initial preoperative dose of antibiotic (75 mg of oxytetracycline), and this prophylaxis was maintained for 48 hours.

The animals were immobilized in a dorsal decubitus position with cervical hyperextension; the operative area was shaved and disinfected, and a surface analgesia of 2% mepivacaine (Scandinibsa) was administered. The trachea was dissected by cervicotomy from the thyroid cartilage to the sternal manubrium, 4 cm of which was resected, starting from the first ring. The prosthesis was then anastomosed at the distal portion with continuous 4-0 monofilament polypropylene; the proximal end of the implant was then stitched in the same way. During the entire operation, the animal was maintained in spontaneous respiration with continuous, low-intensity aspiration of the tracheobronchial secretions and bleeding. Between 2 and 3 mm of implant was invaginated into the inside of the trachea in both anastomoses, avoiding excessive tension in suture lines to prevent damage to the submucous capillary plexus.

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Postoperative Studies

Postoperative studies were evaluated as follows:

CLINICAL. Stridor was evaluated at rest and under effort. Presence of infection was determined. Symptoms were related to survival.

ENDOSCOPIC. With the animals under general anesthesia, we performed endoscopic studies using the same technique described in the surgical procedure, with the aid of an Olympus OES-P10 bronchofibroscope. The endoscopic findings were evaluated after 1 month and for the duration of the experiment.

One month after the intervention, we evaluated stenosis of a third of the lumen or less and its location, and the macroscopic appearance of the inner surface; if possible, we evaluated the degree of granulation tissue invasion and epithelialization. For the duration of the study, only animals in which serious stenosis was suspected by clinical and previous endoscopic findings were considered.

RADIOLOGICAL. Radiological studies were performed by linear tomography of the cervical trachea every month. Stenosis degrees were evaluated according to the existence in the radiological image of a 25%, 50%, 75%, or normal lumen.

ANATOMOPATHOLOGICAL. Stenosis degree was evaluated macroscopically following the same quantitative criteria as described in the previous section, as was the location of its level. We recorded whether local infection was present. Morphology of the endoprosthetic surface was assessed with special attention paid to inflammation or granulation tissue and the degree of epithelialization.

Granulation tissue in the inner prosthetic face was examined microscopically to evaluate its hypertrophic appearance, with qualitative consideration of the intermediate stages that could have existed. We also assessed neovascularization of the implant according to vessel existence in the space around the prosthesis, neocapillaries crossing the prosthesis, or neoformation of a rich capillary subendothelial network. The degree of epithelialization of the implant and its type were also studied.

Table 1. Use of Expanded Tracheal PTFE Prostheses: Endoscopic Findings 1 Month After Operation (n = 10)

Variable Tested	No. of Animals
Tracheal stenosis less than one-third of the lumen	
Upper anastomosis	1
Lower anastomosis	0
Center of the graft	2
Invasion by granulation tissue	
0 = Nonexistent	1
1 = Slight	3
2 = Appearing in islands	3
3 = Hypertrophic granulation tissue	3
Epithelialization	
0 = Traces	1
1 = Beginning of epithelialization	3
2 = Advanced epithelialization	4
3 = Total epithelialization	2

PTFE = polytetrafluoroethylene.

Results

Animals were killed according to the clinical and endoscopic findings when we judged that the degree of tracheal stenosis, when it occurred, was incompatible with comfortable survival. Five animals were killed on days 32, 45, 60, 120, and 180; the 5 other animals survived more than 6 months. One month after implantation, stridor at rest was noted in 1 animal and superficial infection was noted in another; after 45 days, 1 case of stridor under effort and 1 of deep infection (mediastinitis) were noted; and after 4 months, 1 case of stridor under effort was noted.

Necropsy showed that stridor was the result of granulation tissue in anastomoses in the early cases, whereas in the later cases the clinical symptom resulted from stenosis in the center of the prosthesis owing to lack of epithelialization in the inner surface. In all cases, stridor was related to a reduction in tracheal lumen to at least one third of its normal diameter.

Table 2. Endoscopy–Radiology Correlation (n = 10)

Animal Survival (mo)	Endoscopy (Location of Stenosis)			Radiology (Tracheal Lumen)			
	Upper	Lower	Center	100%	75%	50%	25%
1	...	1	...	...	...	...	1
1.5	...	...	1	...	...	...	1
2	...	...	...	...	...	1	...
4	...	...	1	...	...	...	1
6	...	...	...	...	...	1	...
>6	...	...	...	...	2	3	...
Total	0	1	2	0	2	5	3

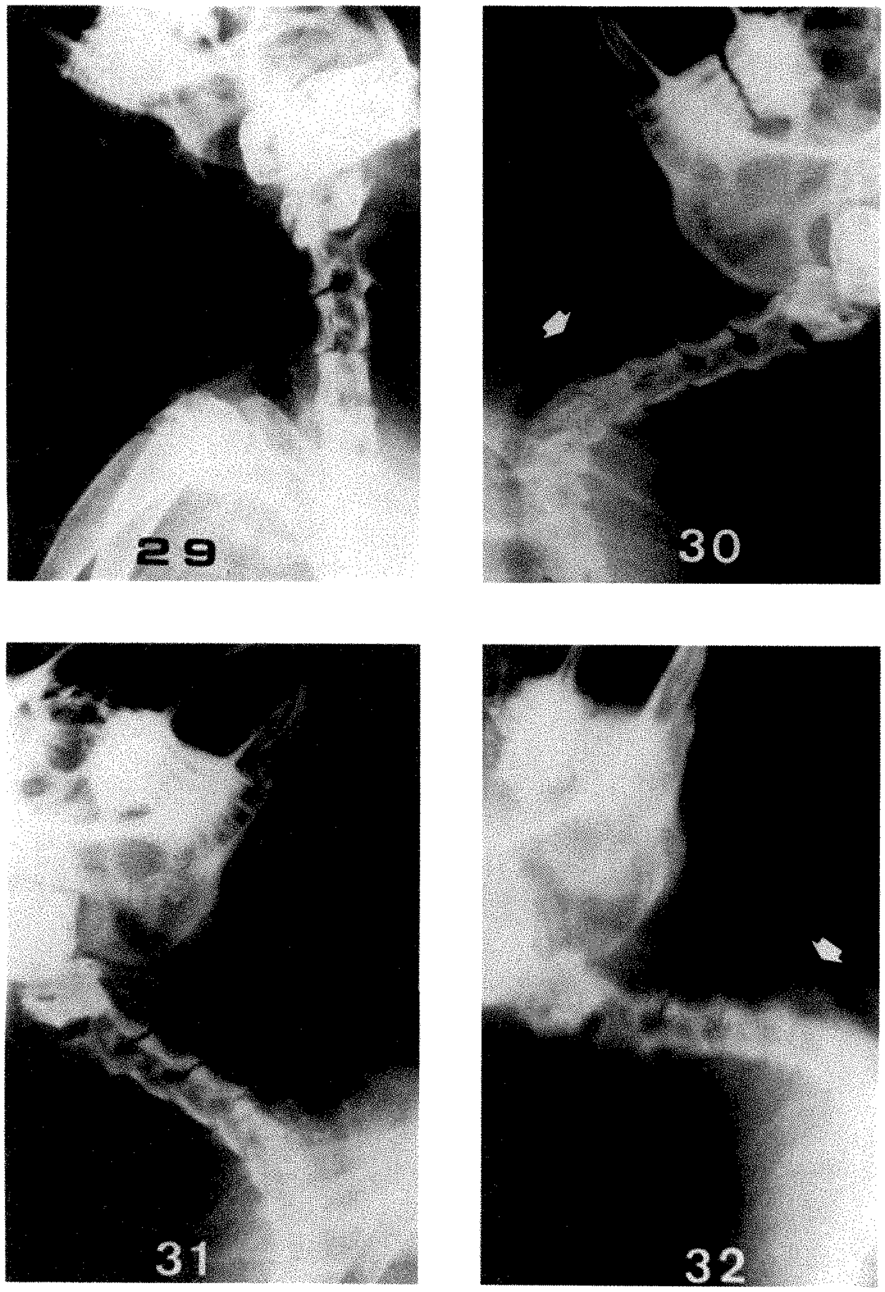

Fig 1. Lineal roentgenography and tomography. Left: The prosthesis was tolerated very well; no stenosis is apparent. Right: prosthesis with stenosis (white arrow).

The endoscopic studies performed 1 month after the surgical procedure showed 3 cases of tracheal stenosis of less than one third of the normal lumen; in 2 animals it was located in the middle of the prosthesis, and in 1 it was located at the level of the lower anastomosis. In these 3 animals we noted granulation tissue and the corresponding clinical symptoms.

Epithelialization of the implant (macroscopically as seen by endoscopy) was complete in 2 animals and greatly advanced in 4 others. Only traces or the beginning of epithelialization was observed in 4 (Table 1).

In the other animals, endoscopy was performed based on the clinical situation and according to radiological images. The tracheal stenosis found in 3 animals after 1 month and suspected after radiology was corroborated. These were the animals killed on days 32, 45, and 120 after implantation (Tables 1, 2).

Early tracheal stenosis was anastomotic owing to technical errors, whereas late lesions occurred at the midportion of the graft secondary to excessive granulation tissue growth and lack of epithelialization.

The radiological images (Fig 1) showed stenosis of more than 25% in the 3 animals described above, and 2 cases of stenosis of about 50% of the lumen. The latter 2 animals underwent postmortem examination after 60 and 180 days. Correlation between endoscopic and radiological findings is shown in Table 2.

Histopathological examination showed macroscopically

Table 3. *Use of Expanded Tracheal Polytetrafluoroethylene Prostheses: Macroscopic Findings (n = 10)*

Animal Survival (mo)	Degree of Stenosis (% of Tracheal Lumen)				Location of Stenosis			Degree of Epithelialization			Introduction of Threads in Lumen			Granulation Tissue[a]					Neovascularization[b]		
	100	75	50	25	Upper	Lower	Center	No	Traces	Total	None	Some	Many	0	1	2	3	4	0	1	2
1	...	...	...	1	...	1	...	1	...	...	...	...	1	...	...	...	...	1	1	...	...
1.5	...	...	...	1	...	...	1	1	...	...	...	1	...	...	...	...	...	1	...	1	...
2	...	...	1	...	...	...	1	...	1	...	...	1	...	...	...	1	...	...	...	...	1
4	...	...	...	1	...	...	1	...	...	1	1	...	...	...	...	...	1	...	...	...	1
6	...	...	1	...	...	...	1	...	...	1	1	...	...	...	...	...	1	...	...	...	1
>6	...	2	3	...	1	...	4	...	...	5	5	...	...	...	...	...	5	...	...	...	5
Total	0	2	5	3	1	1	8	2	1	7	7	2	1	0	0	1	7	2	1	1	8

[a] Presence of granulation tissue on the endoprosthetic surface: 0 = nonexistent; 1 = signs; 2 = almost covering the entire surface; 3 = complete; 4 = hypertrophic. [b] Study of prosthetic neovascularization: 0 = in periprosthesis; 1 = the capillaries cross prosthesis; 2 = rich subepithelial network.

that animals surviving 6 months or more showed a perfect tracheal lumen; a reduced lumen 50% of normal size was observed in only 2 animals. In both, stenosis was located in the middle of the prosthesis.

Regardless of the survival time, some degree of stenosis occurred in the middle of the implant in 5 animals, and in the lower anastomosis in only 1. Epithelialization of the internal prosthetic surface was complete in 5 animals. The macroscopic morphology of the endoprosthetic surface was total epithelialization in the 5 animals that survived more than 6 months; epithelialization was observed after 2, 4, and 6 months. In the cases of shorter survival, on days 31 and 45, marked inflammation with coarse granulation tissue was apparent (Table 3).

Macroscopically, we observed a thick scleroinflammatory sheath around the prosthesis and absence of cartilaginous neoformation (Fig 2). No prosthesis was dislodged, in contrast to the findings of other investigators [15] who used nonporous prostheses. They described the fall of the prosthesis into the bed of cicatricial tissue [15]. In some cases, we found inflammatory granulomas at an anastomotic level. In animals with severe stenosis at the level of the suture line (Fig 3), we observed distal retention of secretions, often purulent. Almost without exception, some degree of stenosis was found in the middle of the prosthesis owing to excessive granulation tissue proliferation. In 8 animals, epithelialization was total. In some animals the introduction of suture threads as the result of technical defects in performing the anastomosis led to severe tracheal stenosis (see Table 3).

Microscopically, we observed a close correspondence between findings of hypertrophic granulation tissue and serious tracheal stenosis. Epithelialization, which to a certain extent runs parallel to the degree or length of granulation tissue, was complete in 8 of the 10 animals in the experiment. As for the endoprosthetic covering, we observed that a transition from nonciliated monostratified to ciliated monostratified epithelium occurred, with complete epithelialization occurring only after the sixth week.

Neovascularization and epithelialization of the tracheal implant were studied macroscopically with special interest. Only in 1 animal, killed after 31 days, did we observe formation of neocapillaries only at the level of periprosthesis. In the rest of the animals, capillaries crossed prostheses, and the 8 animals with maximum survival showed the formation of a rich subepithelial capillary network (Fig 4).

Prosthetic neovascularization occurred in three stages: (1) capillaries located in the periprosthesis; (2) capillaries crossing the prosthesis; and (3) finally, appearance of a rich subepithelial network.

Endoprosthetic epithelialization was complete in 7 animals (those with maximum survival) and was very advanced in the animal killed after 60 days, with ciliated monostratified epithelium in the former and nonciliated monostratified epithelium in the latter. The 2 animals with shorter survival showed only traces of a polystratified epithelium (Table 4).

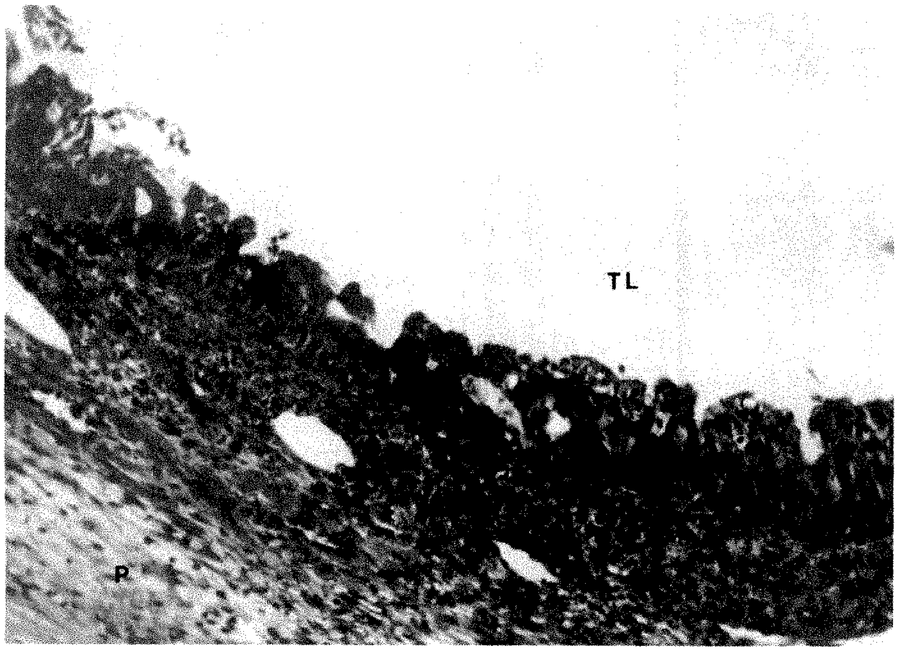

Fig 2. Microphotograph of endoprothesic epithelialization. Histological study 7 months after operation. (GT = granulation tissue; P = prosthesis; TE = traces of epithelium; TL = tracheal lumen.) (Hematoxylin and eosin; ×100 before 29% reduction.)

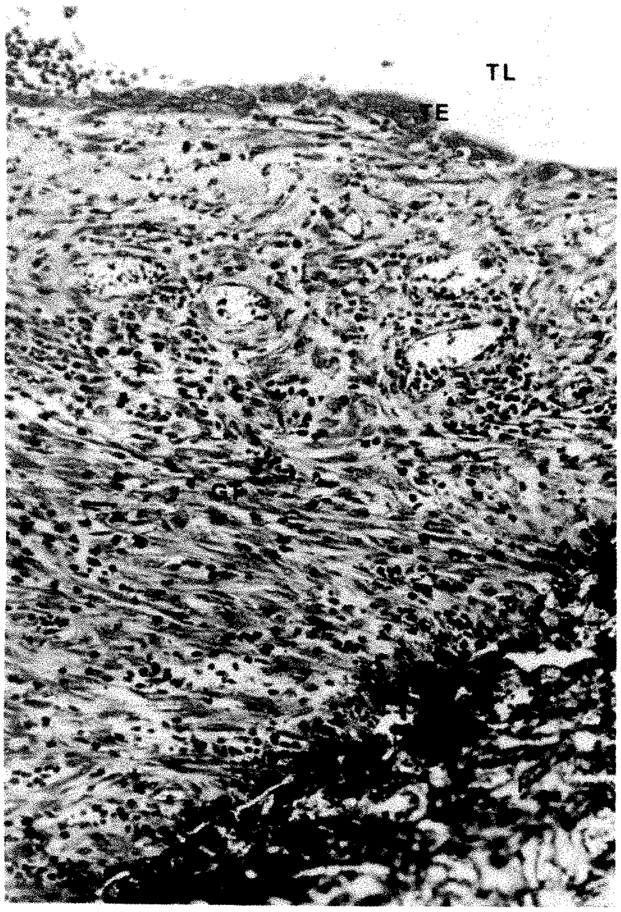

Fig 3. Microphotograph of prosthesis in an animal that died as a result of granulation tissue in the middle of the graft from lack of epithelialization. (GT = Hypertrophic granulation tissue; P = prosthesis; TE = traces of epithelium; TL = tracheal lumen.) (Hematoxylin and eosin; ×100 before 30% reduction.)

Comment

The choice of prosthetic grafts in repair of tracheal stenosis is controversial. The qualities required for a tracheal prosthesis to be considered ideal are impermeability to air, a consistency that prevents collapse, and good acceptance by host tissue causing a minimum inflammatory reaction and always allowing fibroblastic infiltration to occur before epithelialization of the inner surface occurs [16, 17].

We believe that the prosthesis we used has all these qualities. First, the synthetic material, PTFE, is a polymer with an inert component of only 20%; the other 80% is air, which explains its good tolerance. Second, the microporosity (30-μm diameter) is exactly that which allows fibroblastic and therefore vascular invasion, maintaining the necessary aerostasis and avoiding permeation of septic material to the outside. This favors formation of a rich capillary network in submucosa, which allows quick epithelialization. Third, the porous material is hydrophobic, which prevents absorption of water and septic secretions of the tracheobronchial tree except under pressure, impossible in the physiological conditions of the tracheobronchial tree. This explains the low incidence of mediastinitis. Fourth, it is easy to handle in surgery. Finally, the external support of silicone prevents its collapse (Fig 5).

The origin of epithelium in porous prostheses is a matter of debate, variously explained by growth of resection edges or by migration of conjunctive elements through the microporosity, mainly fibroblasts, forming a new submucosa layer or from the vessels (subendothelial network). Thus, in this type of PTFE prostheses, which have been studied mainly as vascular implants, it is supposed that the origin is growth in both anastomotic zones [18], starting from the microcapillaries introduced through the interstices of the implant or from endothelial microemboli that colonize the prosthesis [19]. By histo-

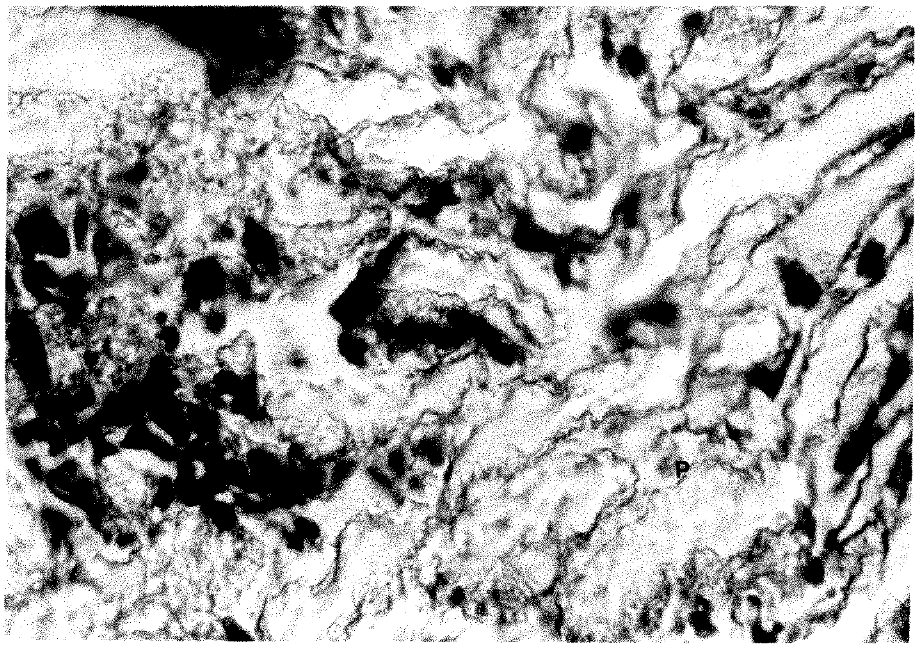

Fig 4. Neovascularization through the prosthesis. (BV = blood vessel; P = prosthesis.) (Masson stain, ×200 before 29% reduction.)

chemical and inmunohistochemical methods and by autoradiography with marked timidine and indium [20], endothelialization in PTFE prostheses has been demonstrated to occur mainly from the resection edges, progressively covering the implant until the middle is reached. Transmural invasion by neoformed capillaries, however, makes these prostheses endothelialize earlier, because these cells also derive from the capillaries that invade the implant [18, 21, 22].

Our preliminary studies at the level of the respiratory tract showed an earlier epithelialization than that described in other studies with other types of prosthesis. This vascular invasion was closely dependent on the microporosity of the material. This fact is very important in understanding why these implants are so well accepted. The epithelial or endothelial growth from the resection edges is limited, and in most experimental models is never complete. If the microporosity allows vascular invasion, however, epithelialization is complete and quick.

With this experimental model, the survival rate using this type of prosthesis was very acceptable, as 50% of the animals survived more than 6 months. Without reaching definitive conclusions, we are aiming to start a new line of research in this difficult area of circumferential tracheal substitutes. Both experimentally and in human clinical practice [11], late cases of degeneration of synthetic material have been demonstrated; therefore, although in our experience "bioincorporation" of such material at the level of the respiratory tract was adequate, clinical controls should be performed indefinitely.

We conclude that use of PTFE externally supported prostheses with silicone rings at the tracheal level achieves better results than does use of any other material

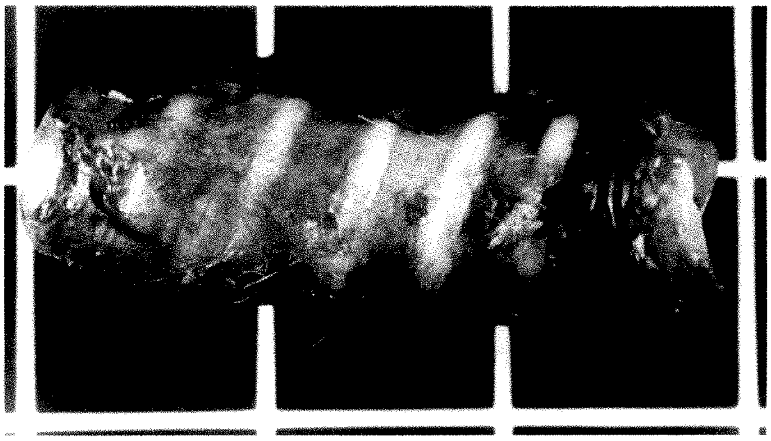

Fig 5. Macrophotography of animal that survived more than 6 months (note perfect bioincorporation of prosthesis and anastomosis lines). (Each square is equal to 1 cm.)

Table 4. Use of Expanded Tracheal Polytetrafluoroethylene Prostheses: Microscopic Findings (n = 10 Animals)

Animal Survival (mo)	Epithelialization				Type of Epithelium		
	Traces	Beginning	Advanced	Complete	Polystratified	Nonciliated monostratified	Ciliated monostratified
1	1	. . .	. . .	. . .	1	. . .	. . .
1.5	1	. . .	. . .	. . .	1	. . .	. . .
2	. . .	. . .	1	. . .	. . .	1	. . .
4	. . .	. . .	. . .	1	. . .	. . .	1
6	. . .	. . .	. . .	1	. . .	. . .	1
>6	. . .	. . .	. . .	5	. . .	. . .	5
Total	2	0	1	7	2	1	7

reported in the literature and that further investigation in this field can achieve good results in human tracheal surgery.

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Paraplegia Associated With the Use of Oxidized Cellulose in Posterolateral Thoracotomy Incisions

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Three patients suffered permanent neurologic injury after oxidized regenerated cellulose migrated into the spinal canal after thoracotomy. These cases are reported to alert surgeons of this potential complication when oxidized cellulose is used to achieve hemostasis in the posterior angle of the thoracotomy incision.

(Ann Thorac Surg 1990;50:288–90)

This report describes 3 patients with paraplegia occurring after a migration of oxidized regenerated cellulose that had been placed in the posterior angle of thoracotomy incisions for hemostasis. Each patient was operated on by a different surgeon between 1981 and 1984 in Houston, Texas. This experience stresses the potential risk of using oxidized cellulose in this manner.

Case Reports

Patient 1

A 72-year-old woman was admitted after discovery of a 2.5-cm lesion in the right mid-lung field on routine chest roentgenography. Bronchoscopic biopsy showed bronchogenic carcinoma. On August 6, 1981, she underwent right upper and middle lobectomy. Histological examination showed poorly differentiated adenocarcinoma, with seven of nine lymph nodes involved with metastatic disease.

For editorial comment, see page 178.

An operation was performed through a routine posterolateral thoracotomy in the fifth intercostal space. The fifth rib was disarticulated from the transverse process to improve exposure and to avoid breaking the rib. Venous bleeding from the posterior angle of the incision was controlled during operation by a laparotomy sponge. After completion of the pulmonary resection and before closure, it was difficult to determine the source of or to control this bleeding. A piece of oxidized cellulose was placed in the posterior angle of the wound near the head of the disarticulated rib. From prior experience, it was believed that wound closure would allow compression of the material against the bleeding vessels and provide hemostasis. The chest wall was closed with large chromic pericostal sutures.

Early in the postoperative period, it was noted that she was unable to move her legs. An emergency myelogram showed a block at the T5-6 level. Emergency laminectomy with cord decompression and evacuation of hematoma was carried out. The evacuated material included a portion of the oxidized cellulose placed in the posterior angle at thoracotomy. With rehabilitation therapy, the patient had a modest return of function but remained essentially paraplegic for a year and a half before she died of metastatic carcinoma.

Patient 2

A 49-year-old man was admitted for resection of a 3-cm nodule in his right upper lobe discovered on routine chest roentgenography not present 18 months before. The results of a percutaneous fine-needle aspiration biopsy were positive for carcinoma. A right upper lobectomy was performed. The specimen showed adenocarcinoma with two of 11 bronchial nodes positive for metastatic carcinoma.

An operation was performed through a right posterolateral thoracotomy in the fifth intercostal space, opened on top of the sixth rib to the tip of the transverse process posteriorly. Venous bleeding from the top of the sixth rib could not be controlled by electrocautery, and the narrow angle precluded ligation of the source. Consequently, one half of a 2 × 14-inch (5 × 36-cm) strip of oxidized regenerated cellulose was folded and placed on top of the sixth rib. After the lung resection was completed, the material was removed. When venous bleeding recurred, the other half of the 2 × 14-inch piece of oxidized regenerated cellulose was placed in the incision as before, and the wound was closed with absorbable pericostal sutures.

The patient's initial postoperative course was uncomplicated, and after extubation, mobilization was begun in the intensive care unit. Neurologic vital signs taken every 2 hours were recorded as normal, and extremity movement was strong for both voluntary motion and movement on command through 48 hours postoperatively. At 50 hours he began to complain of heaviness and numbness in his right leg; but neurologic examination by the intensive care unit resident showed no objective evidence of motor or sensory deficit. When his complaint of right leg numbness persisted 3 hours later, neurologic consultation demonstrated a motor and sensory deficit.

Emergency myelogram showed a complete block at the T5-6 level. Fifty-seven hours after thoracotomy, an emergency laminectomy (T3-6) showed a cord compression by a gelatinous mass consistent with hematoma and oxidized

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cellulose. The mass was partially in the epidural space but extended through the intervertebral foramen laterally. By the time of laminectomy, his neurologic deficit had progressed to involve both legs. After operation, he ultimately regained function in his left leg but continued to have a spastic monoplegia involving his right leg.

Patient 3

A 59-year-old man was hospitalized for resection of an asymptomatic 3-cm nodule in the superior segment of his right lower lobe discovered 2 months previously on a chest roentgenogram obtained after an automobile accident. Bronchoscopy yielded no diagnosis. Operation was performed through a right posterolateral thoracotomy incision in the fifth intercostal space, opened as far posteriorly as possible to avoid rib fracture. Venous bleeding at the posterior angle of the interspace was controlled with oxidized cellulose. A frozen section of the nodule showed a poorly differentiated non-oat cell bronchogenic carcinoma, and a right lower lobectomy was performed. The hemostatic material was removed before wound closure, but bleeding recurred, so a fresh piece was inserted and the ribs were approximated with absorbable pericostal sutures.

When the patient arrived in the intensive care unit 3½ hours later, he was fully awake and complaining of numbness in the lower part of his body and an inability to move either leg. A neurological consultant recommended immediate myelogram, which the patient refused until 6 hours later. Myelogram showed a complete block at the T5-6 level. Laminectomy showed oxidized regenerated cellulose in the spinal canal compressing the cord. Cord decompression resulted in no neurologic improvement.

Comment

Paraplegia after thoracotomy is a rare complication. It has been seen both with and without compressing hematomas, the latter cases presumably on an ischemic basis [1]. The patients described here point out a previously unrecognized risk associated with the use of oxidized cellulose at the posterior angle of the thoracotomy incision. Features common to all 3 patients are the occurrence of venous bleeding that was easily controlled with an absorbable hemostatic material believed to have been used in a completely proper and safe manner. Each surgeon was careful not to pack or compress the material into the angle, and each avoided pushing the hemostatic material into the intervertebral foramen or through it into the epidural space. Yet, in each case, at the time of laminectomy, the oxidized cellulose was found in the spinal canal.

Perez-Guerra and Holland [2] reported a case of postpneumonectomy paraplegia due to epidural hematoma formation. The complication was thought to have been caused by oxidized cellulose blocking the egress of intercostal arterial bleeding. In the patients reported here, the oxidized cellulose itself was apparently causing or contributing to the compression.

Product information warns against leaving this material in situ in laminectomy wounds or in foramina in bones when hemostasis is obtained because swelling can cause nerve damage owing to pressure in a bony confine [3]. No mention is made concerning the potential of the material to migrate. Dutton and associates [4] reported a case of compressive optic neuropathy after oxidized cellulose migrated from the anterior cranial fossa into the orbital apex through an orbital roof fracture. Tashiro and colleagues [5], in an article about complications of epidural anesthesia, describe the migration of oxidized cellulose pledgets into the epidural space. The pledgets were used to pack a rib fractured during thoracotomy. I believe that in the 3 patients reported here, oxidized regenerated cellulose migrated from the posterior angle of the thoracotomy into the spinal canal through the intervertebral foramen. Possible mechanisms of this migration may include pressure created by closure of the ribs with pericostal sutures or respiratory movement itself. Cord compression symptoms may occur early, as in patients 1 and 3, or may be delayed 50 hours postoperatively, as in patient 2.

Use of oxidized regenerated cellulose in the posterior angle of posterolateral thoracotomy incisions presents a risk not previously recognized. Three different experienced thoracic surgeons used the product in a manner believed to have been consistent with the directions of the manufacturer yet with disastrous consequences. To facilitate exposure in posterolateral thoracotomies, dissection is often carried far anteriorly or posteriorly in the intercostal space. Alternatively, ribs may be cut or resected partially or completely. This may avoid some posterior dissection.

However, when bleeding encountered in the posterior angle is uncontrollable by electrocautery or suture ligation, hemostasis achieved using oxidized regenerated cellulose left in situ but unsecured may be accompanied by the risk of migration and neurologic injury.

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INVITED COMMENTARY

In separate communications, Walker and Short have brought to our attention important points relating to the technique of posterolateral thoracotomy. Short has entitled his report "Paraplegia associated with the use of oxidized cellulose in posterolateral thoracotomy incisions." In 1 patient, rib disarticulation from a transverse process was used to improve exposure and to avoid rib fracture. In the other 2 patients, venous bleeding occurred after the intercostal space was opened to the level of the transverse process. In all 3 patients, the goal of the method of incision was to gain exposure and to avoid rib fracture; the fundamental problem was bleeding that resulted in spinal cord compression. Thus, the issue is how to prevent and treat bleeding at the costovertebral angle during thoracotomy. Short's focus is on the avoidance of foreign material that was thought to migrate and to compress the spinal cord. In my judgment, it is the persistent bleeding and not the foreign material that deserves primary attention. Because I know of another patient who suffered paraplegia under similar circumstances from a thoracotomy incision, I presume the complication may be more common than previously reported.

The principles of prophylaxis, diagnosis, and management are: (1) the spinal cord is contained in a fortresslike closed space, and the intervertebral foramina are the peepholes; (2) the thoracic spinal cord blood supply is precarious, and this region is therefore sometimes referred to by neurological surgeons as a "watershed area"; (3) anticipation of the possibility of spinal cord compression is fundamental to taking preventive steps; (4) operations in the paravertebral region include the risk of spinal cord compression; (5) spinal cord compression demands prompt recognition and treatment.

In the management of posterior mediastinal neurogenic tumors, the above principles are well recognized, and collaboration with neurological surgeons is customary. Preoperative computed tomographic scanning and sometimes magnetic resonance imaging are standard. It is usual to gain control of any intravertebral portions of tumors before dissecting the thoracic portions. This approach recognizes the fact that the costovertebral region is a delicate territory wherein neurological surgeons more commonly operate than most thoracic surgeons.

Thoracotomy incisions are generally done quickly, using techniques that are different and rougher than those used around the spinal cord. Within every senior thoracic surgeon's memory is the era when rib(s) were routinely cut or removed. Now, in most centers, ribs are removed or cut uncommonly. Gradual spreading of the ribs, subperiosteal incisions, muscle-sparing incisions, and other adjuncts have made thoracotomies less traumatic than in the past. Nonetheless, oozing at the posterior aspect of the incision is common. The use of a headlight has improved my visibility and my ability to obtain precise hemostasis in the costovertebral angle. When it is occasionally necessary to gain additional exposure, I resect a short segment or even a whole rib. I cannot agree with the routine practice of disarticulation of a rib, particularly without direct vision. Unexpected rib fracture is an acceptable occasional undesirable consequence of thoracotomy that can be quite well handled either by excising a short segment of rib to avoid overriding potentially painful edges or by suture stabilization of the fracture. An extra 5 to 10 minutes devoted to maneuvers that will insure hemostasis in the costovertebral angle is time well spent.

Under circumstances requiring extensive dissection in the costovertebral angle, precise technique is imperative. Should uncontrolled or poorly controlled bleeding in an intervertebral foramen be considered a risk during preoperative assessment, or should it occur unexpectedly, calling for consultation from a neurological surgeon is indicated.

Walker and Short have both provided an important service by calling intravertebral bleeding as a consequence of thoracotomy incision to our attention. Under rare circumstances, when prophylaxis does not suffice to avoid the problem, prompt neurosurgical decompression and hemostasis is indicated.

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Presumed Kawasaki Disease Resulting in Multiple Coronary Artery Aneurysms in an Adult

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Kawasaki disease (mucocutaneous lymph node syndrome) is a pathological process seen mostly in children, but has been reported in adults. The late manifestations of the syndrome can include the development of multiple coronary artery aneurysms. This article describes a 27-year-old man with no risk factors for atherosclerotic disease with multiple coronary artery aneurysms.

(Ann Thorac Surg 1990;50:291–3)

A 27-year-old man with no family history of atherosclerotic disease and associated risk factors was examined by his physician for stabbing chest pain associated with hiking. The patient had no previous history of chest pain or heart disease. The patient also denied any history of extended febrile episodes, adenopathy, oropharyngeal lesions, or abnormal skin changes. An electrocardiogram when the patient was at rest showed nonspecific ST segment changes and Q waves in leads II, III, and aVF. Exercise tolerance test to 90% of maximal heart rate was interpreted as negative. Doppler echocardiography showed moderate mitral valve prolapse and mild leaflet thickening, moderately dilated left ventricle, and a normal aortic valve. The patient was given a regimen of propranolol, and a subjective decrease in chest pain was noted.

The exercise tolerance test was repeated with the patient on a propranolol regimen approximately 4 months later. The patient was subjected to stress to less than maximal heart rate (151 beats/min), and at 8 minutes he had chest pain with 2-mm ST segment depression in leads V_2 through V_5.

An exercise tolerance test with thallium was performed and was interpreted as markedly positive with 4-mm ST changes and chest pain. The thallium report suggested anteroseptal and inferior wall ischemia. Left ventricular catheterization showed aneurysmal dilatation of the left and right main coronary arteries and 100% occlusion of the left anterior descending coronary artery after the first septal branch. The right coronary artery was noted to be tortuous (Figs 1 and 2). The ventriculogram showed an

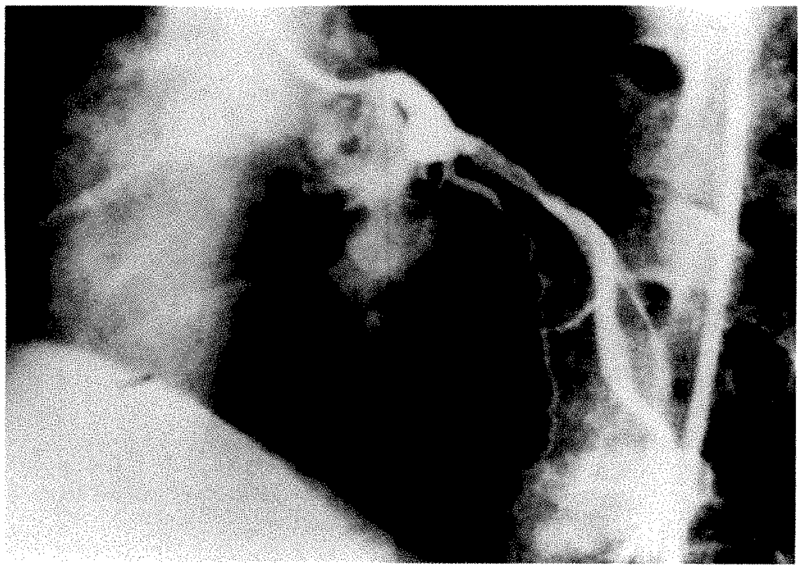

Fig 1. Left coronary injection showing aneurysm and anterior descending artery occlusion.

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The opinions expressed herein are those of the authors and do not purport to express the opinions of the United States Air Force or the Department of Defense.

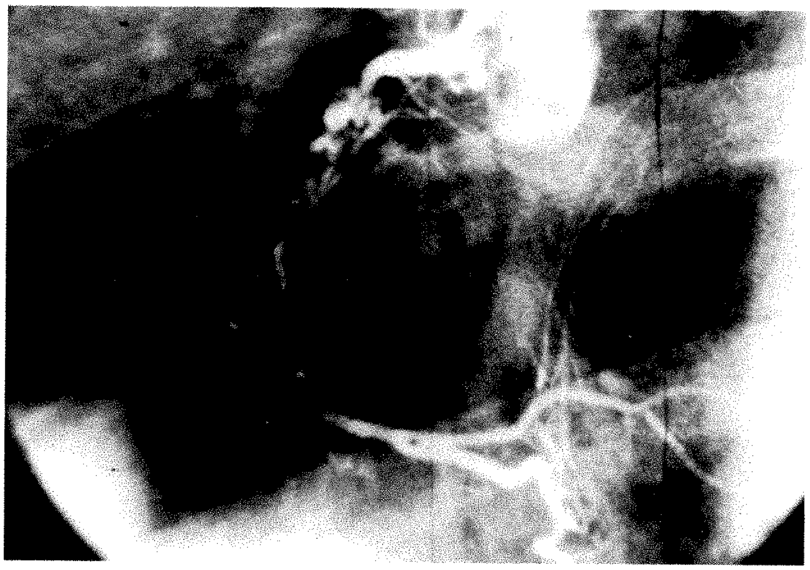

Fig 2. Right coronary artery injection showing proximal aneurysm. Faint visualization of the distal anterior descending artery is seen.

ejection fraction of 0.50 with anterolateral, posterobasal, and posterolateral dyskinesis. Hypokinesis was seen in the apical, basal septal, and apical septal regions. Hemodynamic studies were normal.

At operation, the left internal mammary artery was anastomosed to the left anterior descending coronary artery distal to the aneurysm and the occlusion. The right internal mammary artery was anastomosed to the right coronary artery distal to the aneurysm. A saphenous vein graft was used to bypass the obtuse marginal artery, and the proximal circumflex artery was ligated to prevent embolization from the aneurysm and also to limit competitive flow. The coronary arteries appeared normal at the bypass sites. The patient did well postoperatively and was discharged without complication. On follow-up at 6 months, the patient was stressed with a thallium exercise tolerance test for 11 minutes and had no chest pain, electrocardiographic changes, or evidence of reversible ischemia.

Comment

Although atherosclerosis is the most common cause of coronary artery aneurysms in the United States, Kawasaki disease is the most common cause of nonatherosclerotic coronary artery aneurysms in the US and worldwide [1]. Kawasaki disease can be divided into an acute, subacute, and convalescent phase. The acute phase involves a persistent fever for more than 5 days, exanthema, and oropharyngeal inflammation. The subacute phase is seen with resolution of the patient's fever and desquamation of the skin from distal extremities. It is during this subacute phase that cardiac dysfunction or coronary artery aneurysms may develop. The convalescent phase is characterized by resolution of symptoms [2].

Coronary artery aneurysm develops in only 10% to 20% of patients, and 50% of the aneurysms may regress in 1 to 2 years [3]. Ischemic heart disease is seen in less than 3% of all patients [3]. Sudden death has been reported as caused by thrombosis of these persistent coronary artery aneurysms. Coronary artery bypass grafting has therefore been used for patients with major myocardial ischemia and/or aneurysms that appear to be at risk for thrombosis.

A review of the literature showed at least 9 cases of documented or suspected Kawasaki disease in adults in the US [4]. Although most of these patients do not require coronary artery bypass grafting, it has been reported as successful in the US and Japan [4, 5].

We conclude that young adults with coronary artery aneurysms who have no history of atherosclerotic disease should be questioned about any childhood illnesses resembling Kawasaki disease. We also suggest that a diagnosis of presumed Kawasaki disease should be considered, even if the childhood history is negative for the disease. Coronary bypass grafting may become necessary for the treatment of the coronary artery abnormalities that may occur.

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INVITED COMMENTARY

A report is presented of a 27-year-old man with no risk factors for atherosclerotic disease who subsequently underwent operation for presumed Kawasaki disease resulting in coronary aneurysms and obstructions. Although there was no history suggestive of acute phase of the disease, angiograms of this patient look very similar to those of coronary artery lesions in Kawasaki disease, ie, a recanalized right coronary artery, an occluded left anterior descending artery, and formation of coronary artery aneurysms. Before Kawasaki disease had become widely known in the US, several articles reported surgical treatments for coronary artery aneurysms and obstruction in young adults as cited in our previous publication [1]. The cause of the disease was described as unknown, inflammatory, or congenital at that time. The angiograms presented all closely resembled those of Kawasaki disease, but this cannot be confirmed. In my opinion, these cases should be categorized as "presumed" or "atypical" cases of Kawasaki disease, which are found also in Japan.

Concerning the surgical treatment for this patient, I agree with Brevard and Smith as to the use of bilateral internal mammary arteries anastomosed to the right and left anterior descending arteries [2], although postoperative angiographic studies have not been reported. However, I disagree with the management of the circumflex artery. They described that the circumflex artery, which had been bypassed with a saphenous vein graft, was ligated proximally to prevent embolization from the aneurysm. The simple presence of a small solitary aneurysm as seen in the circumflex artery of this patient does not produce ischemia in the area, and if coronary artery stenosis with a resultant pressure gradient occurs at the inflow or outflow portion of the aneurysm (the most common sites of occlusion in Kawasaki disease), blood flow runs through the graft upward to the aneurysm and thus distal embolization from the aneurysm does not occur, not only theoretically but from our experiences as well. Moreover, grave concern exists regarding the potential late closure of the saphenous vein graft to the artery ligated proximally. No single case has been reported of a ruptured coronary artery aneurysm in the convalescent phase of Kawasaki disease; thus, in my opinion, ligation or resection of the aneurysm is unnecessary. This disease has recently gained much attention [3] in the US, and I congratulate Drs Brevard and Smith on their interesting article.

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Coronary Revascularization in a Child With Kawasaki Disease: Use of Right Gastroepiploic Artery

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In coronary insufficiency produced by Kawasaki disease, myocardial revascularization using saphenous vein, internal mammary arteries, and a combination of both grafts has been performed with considerable success. Recently, we successfully used a right gastroepiploic artery as another conduit in coronary revascularization of a 6-year-old boy with Kawasaki disease. Use of the gastroepiploic artery was feasible even in a small child, and this technique is expected to contribute to long-term graft patency as an arterial graft adjunct to internal mammary arteries.

(Ann Thorac Surg 1990;50:294–6)

Coronary aneurysms and subsequent stenoses produce serious problems in children with Kawasaki disease. After the first successful surgical case [1], many children have been revascularized using saphenous vein grafts (SVGs). However, the mid-term or long-term graft patency of these patients was considerably lower than expected [2]. In 1984, Kitamura and associates [3] first used the left internal mammary artery (IMA) for revascularization of a child with Kawasaki disease, and the use of IMA became the procedure of choice since then. However, IMA has its limitations in number and in length required to reach the posterior surface of the heart. Recently, we applied gastroepiploic artery (GEA) to bypass the posterior descending (PD) branch of the right coronary artery (RCA) in coronary artery bypass grafting of a child with Kawasaki disease.

The patient was a 6-year-old boy in whom Kawasaki disease developed at the age of 3½ years. The first cardiac catheterization performed when he was 4 years old showed huge aneurysms at both coronary ostiums. After the recurrence of Kawasaki disease, he began to experience occasional chest oppression or pain. His second coronary angiography at 6 years showed total occlusion of

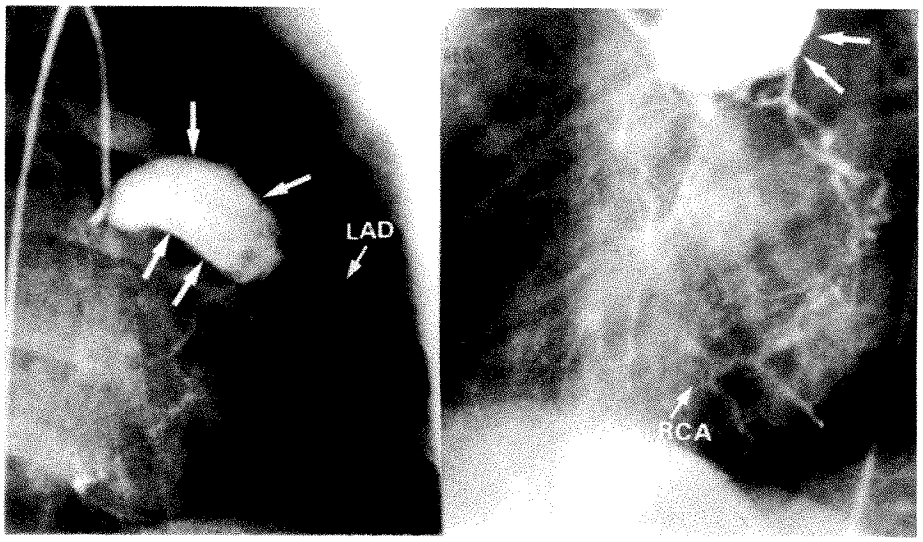

Fig 1. Preoperative coronary angiogram. Right coronary artery (RCA) was totally occluded and opacified by collateral circulation from the circumflex system. Left anterior descending coronary artery (LAD) was also seen by collateral filling from huge aneurysms of the left coronary artery (arrows).

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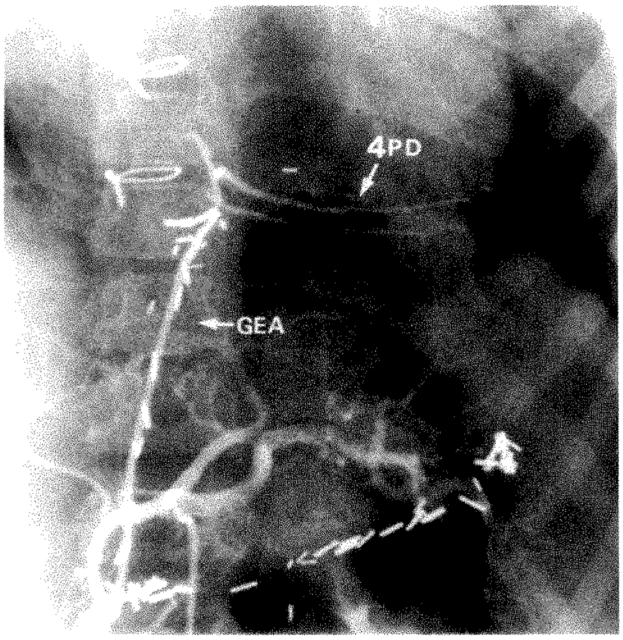

Fig 2. Early postoperative angiogram: right gastroepiploic artery (GEA) anastomosed to posterior descending branch of right coronary artery (4PD) was patent.

the RCA at its origin and a huge aneurysm at the left main coronary artery. The left anterior descending (LAD) and posterior descending branches of the RCA (4PD) were opacified by the collateral circulation from the circumflex system, of which the obtuse marginal branch also had 90% stenosis (Fig 1).

The ejection fraction of the left ventricle was 0.56. The patient's electrocardiogram when at rest was normal, but a treadmill test was positive at the second stage of Bruce protocol owing to chest pain and considerable ST depression in leads II, VI, and V5. The thallium 201 myocardial scintigram showed transient ischemia at LAD and RCA areas. Surgical treatment was advised based on these findings.

At operation, large aneurysms were noted at both origins of the coronary arteries and also just before the bifurcation of 4PD and the atrioventricular branch of RCA. Before cardiopulmonary bypass was begun, the left IMA, GEA, and SVG were prepared and showed good quality. Using moderate hypothermia (25°C) and blood cardioplegia, we first anastomosed SVG to the obtuse marginal branch with interrupted 7-0 silk suture, then the left IMA to LAD and GEA to 4PD with continuous 8-0 polypropylene sutures.

Weaning from cardiopulmonary bypass was easy, and postoperative recovery was smooth without any complications. The postoperative angiogram at 1 month showed that both arterial grafts, GEA to 4PD and LIMA to LAD, were patent, but the SVG-to-obtuse marginal branch graft was occluded (Figs 2, 3). The failure of the SVG-to-obtuse marginal branch graft in this case was attributed to the small perfusion area of this branch and the inability to use IMA because of length. The treadmill test and thallium 201 myocardial scintigram performed 3 months after operation showed considerable improvement of myocardial ischemia at the area of LAD and RCA. The left ventricular ejection fraction was 0.62. The patient was recatheterized 1 year after operation confirming both grafts' excellent patency.

Comment

Since the first report of aortocoronary bypass grafting in a child with Kawasaki disease [1], SVG has been used as a bypass conduit in many cases [4, 5]. It was of great concern from the beginning, however, whether the graft remains patent over the long term in spite of child growth, bypass to inflammatory coronary arteries, and

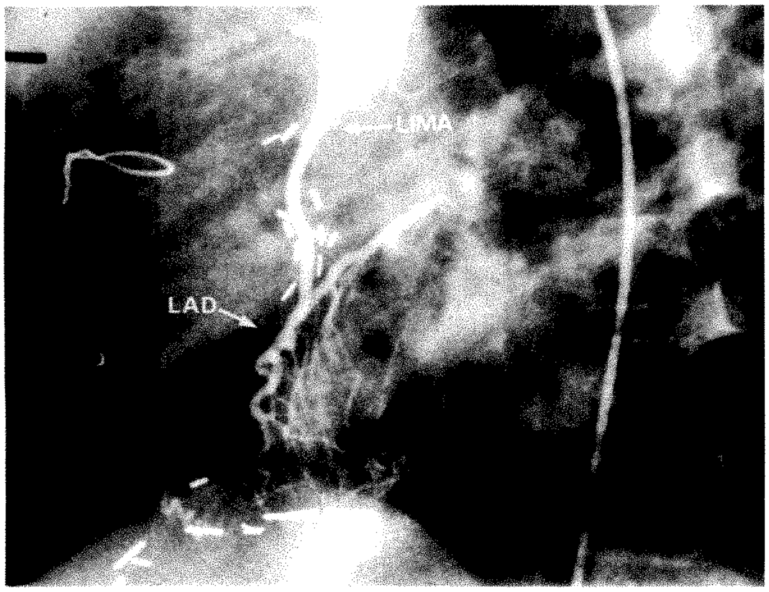

Fig 3. Early postoperative angiogram: the left internal mammary artery graft (LIMA) to anterior descending coronary artery (LAD) was patent.

the specific metabolism of children. Takeuchi and associates [2] reported short-term and relatively long-term graft patency, which were 88% at 1 month (n = 11) and 55% at 5 to 9 years after operation (n = 7) in 11 patients. Owing to the disappointing attrition rate of SVG, IMA has been used in Kawasaki disease whenever feasible since 1984 [3]. Many patients have been operated on using left IMA grafts to LAD and SVG grafts to other coronary branches [2, 5].

Subsequently, the use of bilateral IMA has been reported with good results [6]. However, IMA has its own limitations in number and length. In Kawasaki disease, right coronary aneurysms often show multiple and sausagelike appearance reaching beyond the acute margin and are therefore difficult to bypass with IMA. We applied GEA to bypass the distal RCA (4PD) in a child with Kawasaki disease. The modality of using GEA in adult coronary operations has gained much popularity in recent years [7, 8]. In our first patient, the length of GEA was long enough to reach any part of the coronary arteries, and good quality of the anastomosis was confirmed. Similar to IMA, the adaptation of GEA is of major concern in follow-up examinations in the course of the patient's growth. Several saphenous vein grafts in small children with Kawasaki disease have been reported to adjust their length and lumen to the patient's growth for 5 to 9 years. It is assumed that GEA will grow and will have a higher potential to adjust to the patient's development similar to IMA. To confirm this, it is necessary to have serial follow-up angiograms.

In summary, we used GEA as a bypass conduit to revascularize ischemic myocardium due to Kawasaki disease. The procedures were not complicated even in a small 6-year-old boy. The postoperative angiogram, treadmill test, and myocardial scintigram confirmed satisfactory results. Use of GEA as an additional arterial graft to IMA is expected to contribute to long-term graft patency and to good prognoses of the patients with Kawasaki disease.

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Internal Mammary Artery Graft to Pulmonary Vasculature Fistula: A Cause of Recurrent Angina

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Recurrent angina pectoris developed in a 59-year-old man 3 years after coronary artery bypass grafting using the left internal mammary artery. Cardiac catheterization showed a fistula between the left internal mammary artery and the pulmonary vasculature. This is an unusual documented case of postoperative internal mammary artery graft to pulmonary vasculature fistula after coronary artery bypass grafting. Division of this fistulous communication resulted in resolution of the patient's angina.

(Ann Thorac Surg 1990;50:297–8)

Arteriovenous fistulas of the internal mammary artery are rare. They can be classified as congenital or acquired. Thoracic trauma and iatrogenic injury to the internal mammary artery are the most common causes of acquired fistula. We report an unusual case of acquired internal mammary artery pedicle graft fistula to the pulmonary vasculature after coronary artery bypass grafting.

A 59-year-old man with a history of hypertension and angina pectoris who underwent coronary artery bypass grafting 3 years earlier was admitted for evaluation of recurrent substernal exertional chest pain. The coronary artery bypass operation included a left internal mammary artery graft to the left anterior descending coronary artery and a reversed saphenous vein graft to the posterior descending coronary artery. All coronary artery stenoses were greater than 70%. There was no evidence of perioperative myocardial infarction but the postoperative course was complicated by postpericardiotomy syndrome requiring nonsteroidal antiinflammatory medications for control of chest pain. Recurrent exertional angina 2 years after operation prompted a second cardiac catheterization that showed a patent graft to the posterior descending coronary artery and a patent internal mammary artery graft to the left anterior descending coronary artery.

No fistula was demonstrated at that time; however, selective injection of the internal mammary artery was not performed. The native coronary vasculature demonstrated minimal progression of stenoses. Medical management was initiated and resulted in relief of the patient's chest pain. Angina symptoms were controlled until 3 months before this admission whereupon symptoms recurred with moderate activity. These exertional symptoms increased in frequency and severity shortly before readmission, and the patient was thus admitted for further cardiac evaluation. Exercise stress testing was suggestive of anterolateral ischemia at a low work level (3 mets by Bruce protocol). On admission, the patient was also noted to have a new systolic murmur (2/6) along the left sternal border that had not previously been noted. A second cardiac catheterization was performed. Direct internal mammary artery injection at this study showed an arteriovenous fistula between the left internal mammary artery graft and the pulmonary vasculature of the left upper lobe (Fig 1). The anastomosis between the internal mammary artery graft and left anterior descending coronary artery was patent without stenosis. The native coronary anatomy was unchanged from the previous cardiac catheterization.

Surgical control of this fistula was believed necessary. The fistula was approached through a left anterolateral thoracotomy. Dissection showed dense adhesions between the left upper lobe and the upper mediastinum. To avoid injury to the internal mammary artery graft, the fistula was managed by staple division of the adherent lung from the remaining uninvolved left upper lobe. The patient's angina completely resolved after control of this fistula. Postoperative selective angiography demonstrated brisk flow through the internal mammary artery graft to the left anterior descending artery without residual fistulous communication to the lung (Fig 2). The patient experienced no chest pain or electrocardiographic changes of ischemia with moderate exercise postoperatively.

Comment

Arteriovenous fistulas of the internal mammary artery are uncommon. Senno and colleagues [1], in their review of the subject, classified the fistulas as congenital and traumatic or iatrogenic, with most cases falling into the latter two categories. A fourth category of acquired internal mammary artery fistulas resulting from lymphoid neopla-

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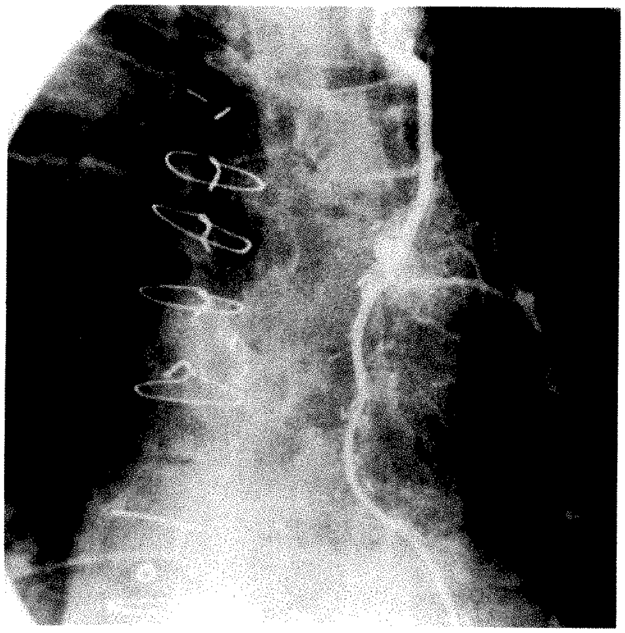

Fig 1. Arteriogram showing fistulous connections between the internal mammary artery and the pulmonary vasculature of the left upper lobe.

sia and chronic granulomatous disease has also been described [2, 3].

Internal mammary artery fistulas after open heart operations are extremely rare with only 4 previously reported cases. These cases involved fistulas between the internal mammary artery and vein and between the internal mammary artery and the thymic and second intercostal veins [4, 5]. All cases were believed to be related to simultaneous internal mammary artery and venous trauma occurring at sternal wire placement. The internal mammary artery pedicle was not used as a coronary bypass conduit in these cases.

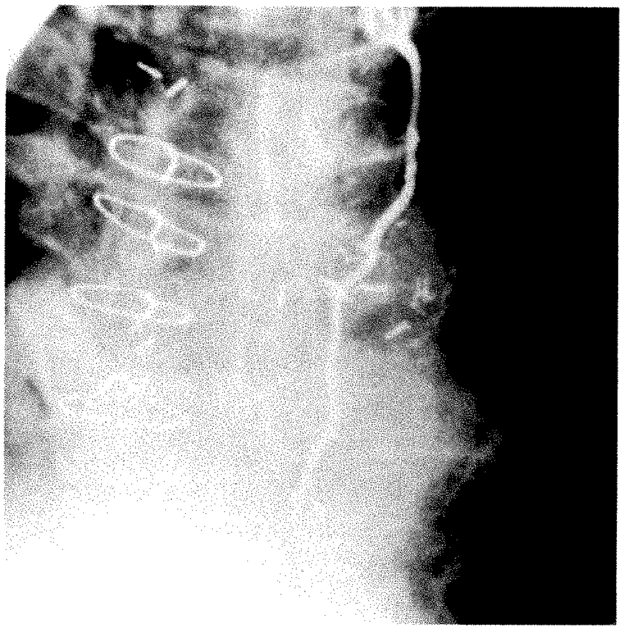

Fig 2. Postoperative arteriogram after division of the arteriovenous fistula demonstrating brisk flow to the coronary circulation.

Internal mammary artery fistulas involving the pulmonary vasculature are most often congenital in origin. Two previous iatrogenic cases involved anterior chest tube placement and closed chest cardiac massage [6, 7]. In the present case an internal mammary artery to pulmonary parenchymal fistula occurred after coronary artery bypass grafting using the internal mammary artery pedicle graft.

As with the more commonly seen peripheral arteriovenous fistula, surgical treatment is indicated to prevent complications of secondary mycotic aneurysm, congestive heart failure, infectious endocarditis, aneurysmal expansion and rupture, or distal ischemia [8]. Our patient's primary complaint was recurrent angina pectoris resulting from a steal of internal mammary flow away from the dependent left anterior descending arterial circulation. These symptoms were progressive in nature, and with time they may have led to an anterior myocardial infarction or congestive heart failure. The pathophysiological importance of this fistula is supported by the relief of ischemic chest pain after its division.

Internal mammary arteriovenous fistula is a rare complication of coronary artery bypass grafting using the internal mammary artery. Such arteriovenous fistulas should be included in the list of possible causes of recurrent angina pectoris after coronary artery bypass grafting using the internal mammary pedicle graft. This is especially the case when a new systolic murmur occurs over the precordium in the postoperative period. Finally, this case emphasizes the importance of selective angiography of the internal mammary artery in the workup of recurrent chest pain after bypass grafting using this conduit.

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Esophageal Perforation in a Patient With Acquired Immunodeficiency Syndrome

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Infection with *Mycobacterium tuberculosis* is frequently found in patients with acquired immunodeficiency syndrome and can result in diffuse lymphadenopathy from disseminated disease. A case is presented of esophageal erosion and perforation secondary to mediastinal lymph node enlargement from *Mycobacterium tuberculosis* in a patient positive for human immunodeficiency virus. Emergent surgical intervention required resection of the perforated esophagus, end-cervical esophagostomy, gastrostomy, and feeding jejunostomy. Long-term prognosis is poor owing to acquired immunodeficiency syndrome, therefore, reconstruction at a later date is uncertain.

(Ann Thorac Surg 1990;50:299–300)

Patients infected with the human immunodeficiency virus (HIV) are prone to have infectious complications and neoplastic diseases owing to impaired immune function. Infectious complications are most often due to reactivation of latent disease, and the overwhelming majority of patients die of repeated infections [1]. Associated complications requiring surgical intervention are not uncommon. A case is presented of an HIV-positive patient with mediastinal lymphadenopathy that ultimately led to esophageal erosion and perforation.

A 21-year-old homosexual man was seen with a 3-month history of malaise, cough, night sweats, and weight loss. The result of his test for HIV 2 years earlier was positive but he had no other qualifying criteria for acquired immunodeficiency syndrome (AIDS). Prior medical history included tuberculosis at age 13 years, for which he was treated. On admission, he was febrile to 38.9°C and had an unremarkable physical examination. Chest roentgenogram showed right hilar and mediastinal adenopathy but no infiltrates.

His presumptive diagnosis was *Pneumocystis carinii* pneumonia versus *Mycobacterium tuberculosis* pneumonia. Treatment for presumed *Pneumocystis carinii* pneumonia was started with intravenous Septra (trimethoprim and sulfamethoxazole; Burroughs Wellcome Co, Research Triangle Park, NC). After 3 days, he continued to have fevers to 39.4°C so an antituberculous regimen was started with isoniazide, rifampin, and pyrazinamide.

On the 17th day of hospitalization, his temperature reached 39.5°C and he had complaints of right-sided chest pain and painful swallowing. There was no further evaluation until 3 days later when an esophagogram was obtained showing a perforation (Fig 1) of the proximal intrathoracic esophagus. A surgical consultation was called, and the patient was promptly taken to the operating room.

On arrival, the patient had shaking chills, a temperature of 40°C, and a white blood cell count of 1.9×10^9/L (1,900/μL). A right thoracotomy showed a mediastinal mass of enlarged nodes that were inflamed and edematous. The nodes were resected to gain exposure to the esophagus, and this showed a large perforated segment on the posterior lateral wall that measured 5 cm in length and more than 50% of the esophageal diameter. Treatment required resection of the perforated segment, end-cervical esophagostomy, gastrostomy, and feeding jejunostomy. The patient's sepsis resolved, and he was begun on tube feedings on postoperative day 4. Intercostal drainage catheters were removed by day 10, and the remainder of the postoperative course was uncomplicated.

Final pathological diagnosis of the nodes demonstrated necrotizing granulomas, and the nodal culture stain was positive for acid-fast bacilli. *Mycobacterium tuberculosis* eventually grew in the cultures. There was no intrinsic pathological condition in the esophagus.

Comment

Optimal management of esophageal perforation requires prompt diagnosis and treatment. Several factors influence the eventual outcome in these patients including the cause of perforation, the site (cervical, mid-esophageal, or distal esophageal), and the presence of underlying esophageal disease. However, most important is the time interval between the actual perforation and the institution of therapy. Survival declines markedly if there is a delay of more than 24 hours owing to the onset of sepsis and its complications. Two retrospective reviews by Nesbitt and Sawyers [2] and Bladergroen and colleagues [3] have examined a large series of patients with esophageal perforation within their respective institutions, and both reviews found a marked difference in mortality between patients treated early (less than 24 hours) and those with

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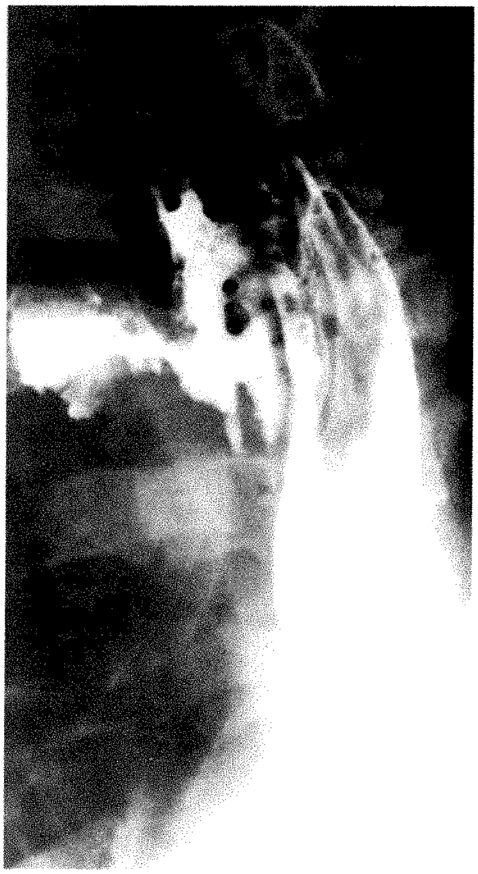

Fig 1. Esophagogram showing large perforation in the proximal intrathoracic esophagus.

delayed intervention (more than 24 hours). In each case, the mortality rate was more than double when therapy was delayed (11% versus 26% and 14% versus 33%, respectively). In addition, the highest mortality was seen in patients with spontaneous perforation, most likely owing to delay in diagnosis.

The patient in this case was known to be HIV-positive at the time of operation but did not carry the clinical diagnosis of AIDS. He did have a prior history of tuberculosis as a child, and in his immunocompromised state, the diffuse lymphadenopathy was a systemic manifestation of reactivated latent disease. Extrapulmonary and disseminated tuberculosis are often found in AIDS patients [4], and the positive stain of the mediastinal nodes for acid-fast bacilli clearly places this patient in the AIDS category by the diagnostic criteria of the Centers for Disease Control [5]. Although mediastinal adenopathy is commonly found under these circumstances, it is highly unusual that it would cause spontaneous esophageal perforation. This appears to be the case, as there was no intrinsic esophageal disease found on pathological sectioning. Most likely, the mass of nodes led to erosion and eventual perforation by pressure necrosis in combination with the inflammatory reaction in the tuberculous nodes. The clinical history indicates that the delay between perforation and operation was 3 days. This correlated to the amount of necrosis, edema, and inflammation found in the mediastinum. These findings, along with the size of the defect, necessitated radical therapy including resection of the perforated segment. Any lesser procedure (ie, primary repair with buttressing or diversion) could cause continued mediastinal soilage that would be poorly tolerated in an immunocompromised patient. This aggressive approach concurs with the recommendations of DeMeester [6] for delayed treatment of esophageal perforation. An acceptable alternative would be a transhiatal esophagectomy with esophagogastrostomy.

This patient has fully recovered from his sepsis, is nutritionally maintained through a jejunostomy catheter, and is awaiting discharge pending placement in a home for AIDS patients. Unfortunately, owing to the extremely poor prognosis associated with AIDS, later reconstruction seems unlikely.

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Primary Mediastinal Leiomyoma

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An elderly woman was seen with a left mediastinal mass in the region of the aortic arch on chest roentgenography. Further imaging with computed tomography, angiography, and magnetic resonance demonstrated a highly vascular neoplasm adjacent to the aortic arch. Pathological analysis of the resected specimen showed a leiomyoma. A brief review of the 10 previous reported cases of primary mediastinal leiomyoma is provided.

(Ann Thorac Surg 1990;50:301–2)

A 75-year-old woman, previously healthy and a nonsmoker, was admitted with a 2-year history of dry cough but was otherwise asymptomatic. Results of physical examination and laboratory tests were normal. Figure 1 shows the posteroanterior chest roentgenogram obtained at this time. This film was initially interpreted as demonstrating an aneurysm of the aortic arch. A computed tomographic study of the chest showed a rounded mass adjacent to the aortic arch measuring 5 × 7.5 cm in diameter and containing scattered tiny areas of calcification. Figure 2 shows a computed tomographic image through the mass after administration of intravenous contrast medium. Thoracic aortography showed no evidence of aortic aneurysm. Magnetic resonance imaging showed the mass to encircle partially the transverse portion of the aortic arch and to produce slight extrinsic compression of the left main bronchus.

The mass was approached through a left posterolateral thoracotomy. It was found to have no connection to the great vessels and esophagus and was easily dissected free of them. The mass derived blood supply from multiple enlarged mediastinal vessels. The patient's postoperative course was uncomplicated, and she was discharged home on the fourth postoperative day. At a follow-up clinic visit 6 months later, her cough had resolved and a second chest roentgenogram showed no evidence of tumor recurrence.

Gross pathological examination of the tumor demonstrated a 5 × 7 × 4-cm, encapsulated, rubbery mass with areas of cystic degeneration and central calcification. Microscopic examination showed a tumor composed of uniform spindle cells with electron microscopic and immunoperoxidase staining characteristics of smooth muscle. Numerous vascular channels were present throughout the tumor.

Comment

Within the mediastinum, leiomyomas usually arise from adjacent structures having smooth-muscle walls, such as the esophagus or great vessels [1, 2]. We report a leiomyoma of the mediastinum arising as a primary mesenchymal tumor in the region of the aortic arch. Only 10 patients with primary mediastinal leiomyomata have previously been reported.

Benign mesenchymal tumors of the mediastinum are rare, representing only 1% to 6% of all mediastinal masses in several large series [3–5]. Of such tumors, leiomyomas are among the least frequent, representing only one of the 22 tumors found in the largest published series of mediastinal mesenchymal tumors [6]. Actual percentages for primary mediastinal leiomyomas are probably even lower, as many older reported cases may represent pedunculated esophageal tumors or neural tumors rather

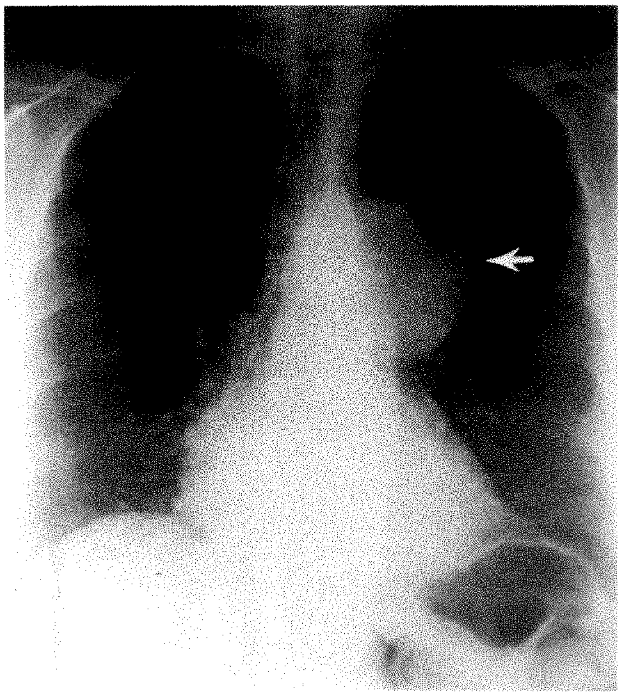

Fig 1. Posteroanterior chest roentgenogram showing a rounded, smoothly marginated mass in the region of the aortic arch (arrow).

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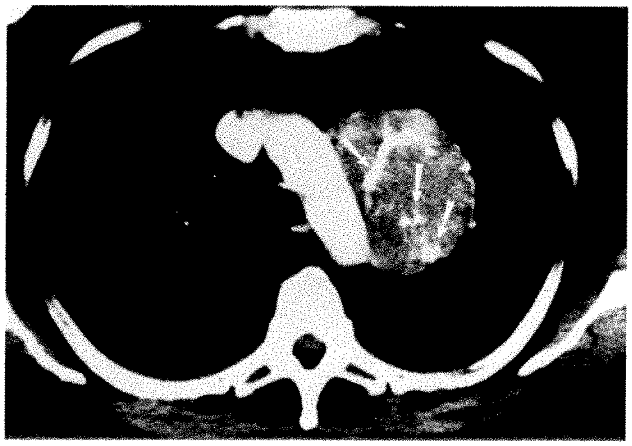

Fig 2. Contrast-enhanced computed tomographic image showing numerous enhanced vascular channels within the mass (arrows).

than true smooth muscle tumors. Among the 6 Japanese cases of primary mediastinal leiomyoma, the posterior mediastinum was the most common location. The tumor was often quite large at the time of diagnosis owing to slow growth and relative lack of symptoms [3, 6, 7]. The age range of patients with primary mediastinal leiomyoma was 22 to 67 years. The tumor was five times as common in female patients as in male patients. Follow-up after 10 years in 1 patient showed no recurrence [7].

In our patient, the location of the tumor adjacent to the aortic arch caused an initial misdiagnosis of aortic aneurysm on chest roentgenography. Further imaging studies were essential for optimal surgical planning. Contrast-enhanced computed tomography, angiography, and magnetic resonance imaging all indicated that the mass represented a highly vascular neoplasm rather than an aneurysm.

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Reversal of Protamine-Induced Catastrophic Pulmonary Vasoconstriction by Prostaglandin E_1

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A case of catastrophic pulmonary vasoconstriction occurring after cardiopulmonary bypass after protamine reversal of heparin treated successfully with intravenous prostaglandin E_1 is reported. Systemic hypotension was counteracted by epinephrine given through the left atrium. Protamine-heparin reactions are reviewed and a pathophysiological mechanism for the beneficial effect seen with prostaglandin E_1 is proposed.

(Ann Thorac Surg 1990;50:303–5)

Catastrophic pulmonary vasoconstriction after cardiopulmonary bypass can occur after protamine reversal of heparin and may lead to serious morbidity [1]. Although the mechanism of this protamine–heparin-induced response is unclear, complement activation and thromboxane release may play a role, particularly in the development of pulmonary vasoconstriction. We describe a case of protamine-associated pulmonary vasoconstriction leading to obstruction of pulmonary blood flow and unresponsive to vasodilators until prostaglandin E_1 was given through the pulmonary artery.

A 63-year-old man was scheduled for aortic valve replacement. Preoperative evaluation showed moderate aortic stenosis and aortic insufficiency, pulmonary artery pressure of 25/10 mm Hg, and pulmonary capillary wedge pressure of 6 mm Hg with a cardiac index of 2.9 L/min. He had no history of lung disease, prior protamine or insulin exposure, fish allergy, or a previous vas ligation. He was not taking acetylsalicylic acid or other cyclooxygenase inhibitors.

The patient underwent aortic valve replacement with a 23-mm St. Jude valve. Bovine heparin (32,000 U, 400 U/kg) was used for anticoagulation. Myocardial protection was achieved by sequential delivery of oxygenated blood cardioplegia every 20 minutes through the coronary ostia. The patient was weaned from cardiopulmonary bypass in normal sinus rhythm on 0.05 μg/kg/min of epinephrine and 0.5 μg/kg/min of nitroglycerin. The central venous pressure was 20 mm Hg, the pulmonary artery pressure was 19/10 mm Hg, and the cardiac index was 1.8 L/min. Protamine (300 mg) was given peripherally over 10 minutes. Subsequently, the central venous pressure rose to 30 mm Hg despite only a minimal rise in the pulmonary artery pressure to 26/14 mm Hg, and global right ventricular dysfunction was noted. An arterial blood gas on 100% oxygen showed a pH of 7.41, a carbon dioxide tension of 41 mm Hg, and an oxygen tension of 176 mm Hg. Tidal volume was 700 mL with a peak inspiratory pressure of 20 cm H_2O.

The patient was reheparinized and placed back on bypass. A right coronary ostial dissection was found and bypassed with a reverse saphenous vein graft. However, the patient now could not be weaned from bypass despite a well-contracting right ventricle, a pulmonary artery pressure of 30/23 mm Hg, and an intraaortic balloon pump. A left atrial line showed the left atrial pressure to be 0 mm Hg despite a simultaneous pulmonary artery diastolic pressure of 23 mm Hg. Direct left ventricular puncture confirmed the left ventricular pressure to be 50/0 mm Hg. Neither epinephrine nor nitroglycerin systemically or via the pulmonary artery was able to reverse the pulmonary vasoconstriction (Fig 1). An arterial blood gas on 100% oxygen failed to implicate hypoxic pulmonary vasoconstriction with a pH of 7.49, a carbon dioxide tension of 33 mm Hg, and an oxygen tension of 221 mm Hg. The tidal volume remained at 700 mL and the peak inspiratory pressure had risen to 30 cm H_2O.

Prostaglandin E_1 (PGE_1; 30 μg) was injected into the main pulmonary artery with an immediate elevation of the left arterial pressure to 6 mm Hg. A second injection of PGE_1 (30 μg) was administered, and a continuous PGE_1 infusion (0.05 μg/kg/min) was started through the pulmonary artery. Systemic hypotension accompanied the administration of PGE_1 and was treated with epinephrine administered through the left atrial line. The patient came off bypass easily with a pulmonary artery pressure of 35/15 mm Hg and left atrial pressure of 10 mm Hg. Again, arterial blood gases on 100% oxygen showed a oxygen tension of 347 mm Hg with a pH of 7.43 and a carbon dioxide tension of 41 mm Hg. Prostaglandin E_1 therapy was associated with an improvement in compliance, the peak inspiratory pressure having decreased to 20 cm H_2O. Recognizing the possibility of exacerbating the pulmonary vasoconstriction, we again used 200 mg of protamine for heparin reversal, but it was given over 1 hour. Blood

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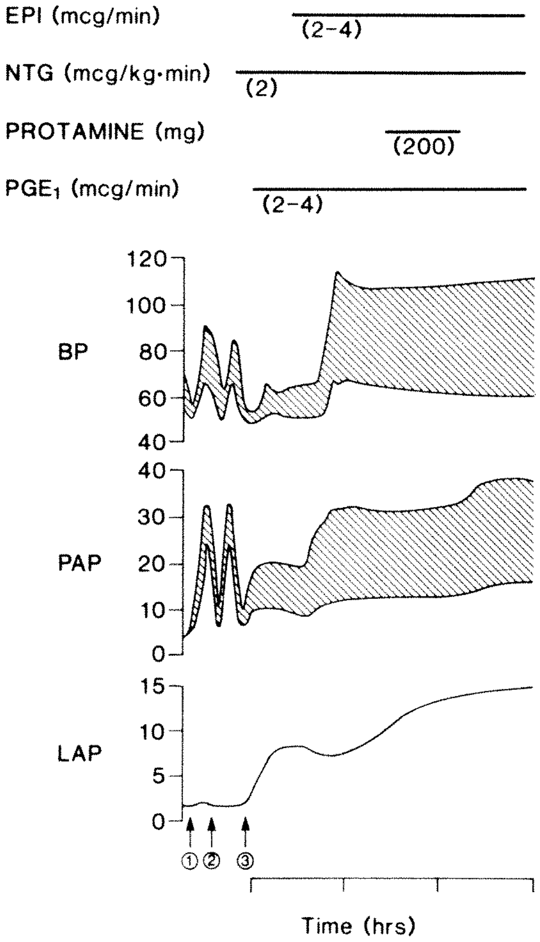

Fig 1. Composite of an intraoperative tracing obtained on a strip chart recorder representing the attempt to wean the patient from cardiopulmonary bypass after the right coronary artery had been bypassed. The graph demonstrates systemic blood pressure (BP), pulmonary artery pressure (PAP), and left atrial pressure (LAP) during attempts 1, 2, and 3 to come off bypass. Note that in the face of high-filling pressures (1 and 2) with and without nitroglycerine (NTG), LAP remained less than 2 mm Hg. However, with the two bolus injections of prostaglandin E_1 (PGE$_1$) (3) and with initiation of a continuous drip, PAP fell markedly, left ventricular preload occurred, and bypass was able to be terminated. (EPI = epinephrine.)

specimens obtained intraoperatively were negative for antiprotamine immunoglobulin G or immunoglobulin E.

Postoperatively, the intraortic balloon pump was able to be weaned the following day along with cessation of the epinephrine and PGE$_1$. The patient thereafter had an uneventful recovery.

Comment

We describe a case of protamine-induced severe pulmonary vasoconstriction causing inadequate left ventricular filling with an inability to wean from bypass. The pulmonary vasoconstriction persisted more than 2 hours after protamine administration. Prostaglandin E_1 reversed the pulmonary vasoconstriction and allowed successful weaning from bypass.

Postbypass reactions to protamine have been characterized into three categories [2]. Type I reactions are characterized by transient systemic hypotension [3]. Type II reactions appear to be an anaphylactoid response to protamine with release of vasoactive mediators from mast cells as a result of antigen–antibody interaction. Antiprotamine immunoglobulin E and immunoglobulin G have been associated with this type of response [4]. Catastrophic pulmonary vasoconstriction is categorized as a type III reaction. This occurs infrequently. It has been reported after cardiopulmonary bypass in 5 patients who had pulmonary artery hypertension, right ventricular failure, and systemic hypotension [1]. Though the mechanism for this reaction has not been well defined, it may be mediated by nonimmunologic complement activation from the heparin–protamine complex [5]. The pulmonary vasoconstriction may be due, in part, to the arachidonic acid metabolites thromboxane A_2 and prostaglandin F_2, both potent pulmonary vasoconstrictors [6, 7]. In animals, this response can be decreased by cyclooxygenase inhibitors and by the oxygen radical scavenger dimethylthiourea [8].

The case reported here appears to be a type III reaction to protamine as the absence of antiprotamine antibodies and the hemodynamic pattern suggest that it was not a type II reaction. In fact, it may have been unrecognized as an exacerbating factor in the right ventricular failure requiring reheparinization and resumption of cardiopulmonary bypass to revascularize the right coronary artery. Our attempts to wean the patient from bypass unveiled massive pulmonary vasoconstriction with virtually no transpulmonary blood flow. Unlike previous reports [1], the vasoconstriction in this patient was persistent and unresponsive to β-agonist and nitrate vasodilators, perhaps as a result of the second cardiopulmonary bypass exposure.

Although it has been used as therapy for pulmonary vasoconstriction in other conditions [10], PGE$_1$ also answers the need of therapy for catastrophic pulmonary vasoconstriction associated with a type III reaction to heparin reversal by protamine. The vasoconstriction in this case was unresponsive to standard vasodilators. Prostaglandin E_1 may be especially useful in this clinical setting, in which vasoconstriction may be thromboxane mediated [11].

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Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1993 may begin the recertification process in 1991. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1991. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Complete Foregut Duplication

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Alimentary tract duplications are rare congenital anomalies with the majority identified in the pediatric age group. However, duplications may be seen in the adult population and require operative excision. A 53-year-old man was seen with vague, nonspecific symptoms and was found to have a complete esophageal and gastric duplication with communication to the normal alimentary tract. Appropriate-for-structure epithelium was noted throughout the length of the duplication.

(Ann Thorac Surg 1990;50:306–8)

True duplications of the structures within the alimentary tract are rare and usually are seen in the pediatric age group. When the duplications in adults are referred to clinical attention, the symptoms are usually vague; however, 85% [1] will require operative intervention to relieve their symptoms. Esophageal duplications predominantly occur in the lower third of the esophagus (60%) with symptoms of dysphagia or epigastric discomfort [2]. Gastric duplications will frequently contain parietal cells, and with secretion of hydrochloric acid may first be seen as peptic ulceration. In the two largest reviews of alimentary tract duplication in adults [1] and children [3], only 3% to 4% were thoracoabdominal duplications. We report a patient with complete esophageal duplication in continuity with a gastric duplication traversing the diaphragm through a separate hiatus.

The patient is a 53-year-old man who had chronic iron deficiency anemia and a vague past history of lethargy, weakness, frequent "pneumonias," and occasional right upper quadrant pain. The patient had been followed up in the past with abdominal ultrasounds, barium swallow and enema, and endoscopy, all of which were nondiagnostic. Recently, the patient again was observed with marked lethargy and with a hemoglobin level of 76 g/L (7.6 g/dL). Physical examination was completely unremarkable except for intermittent hemoccult-positive stools. All laboratory examinations were normal except for low iron and ferritin levels consistent with chronic blood loss. A chest roentgenogram demonstrated a posterior mediastinal air fluid level (Fig 1). An extensive workup of the posterior mediastinal air fluid level and anemia was begun.

Computed tomography of the chest and abdomen demonstrated a large fluid-filled tubular structure alongside the esophagus beginning high in the left posterior mediastinum, extending into the right posterior mediastinum, and entering the abdomen through a diaphragmatic hiatus separate from the true esophageal hiatus (Fig 2). In addition, a round cystic structure was identified under the left lobe of the liver along the lesser curve of the stomach. The remainder of the computed tomographic scan including the spine was normal. External and endoscopic ultrasound confirmed the presence of the thoracic tubular

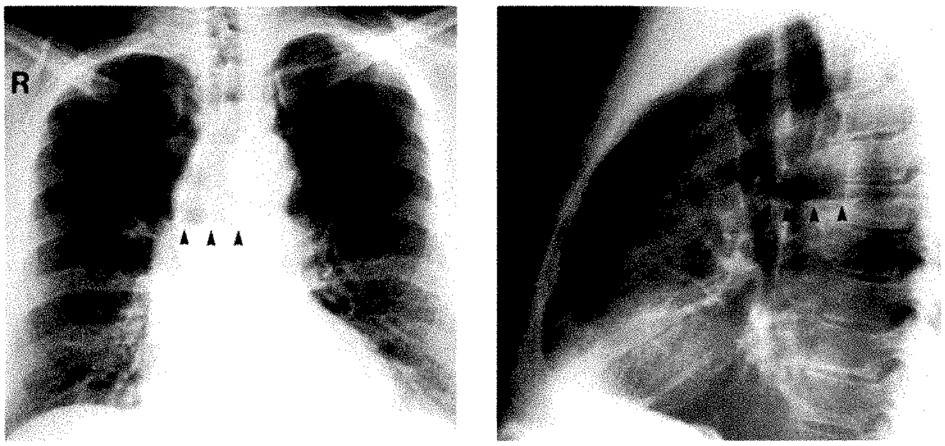

Fig 1. Chest roentgenogram, posteroanterior and lateral views, demonstrates an air fluid level (arrowheads) *in the duplication located in the posterior mediastinum.*

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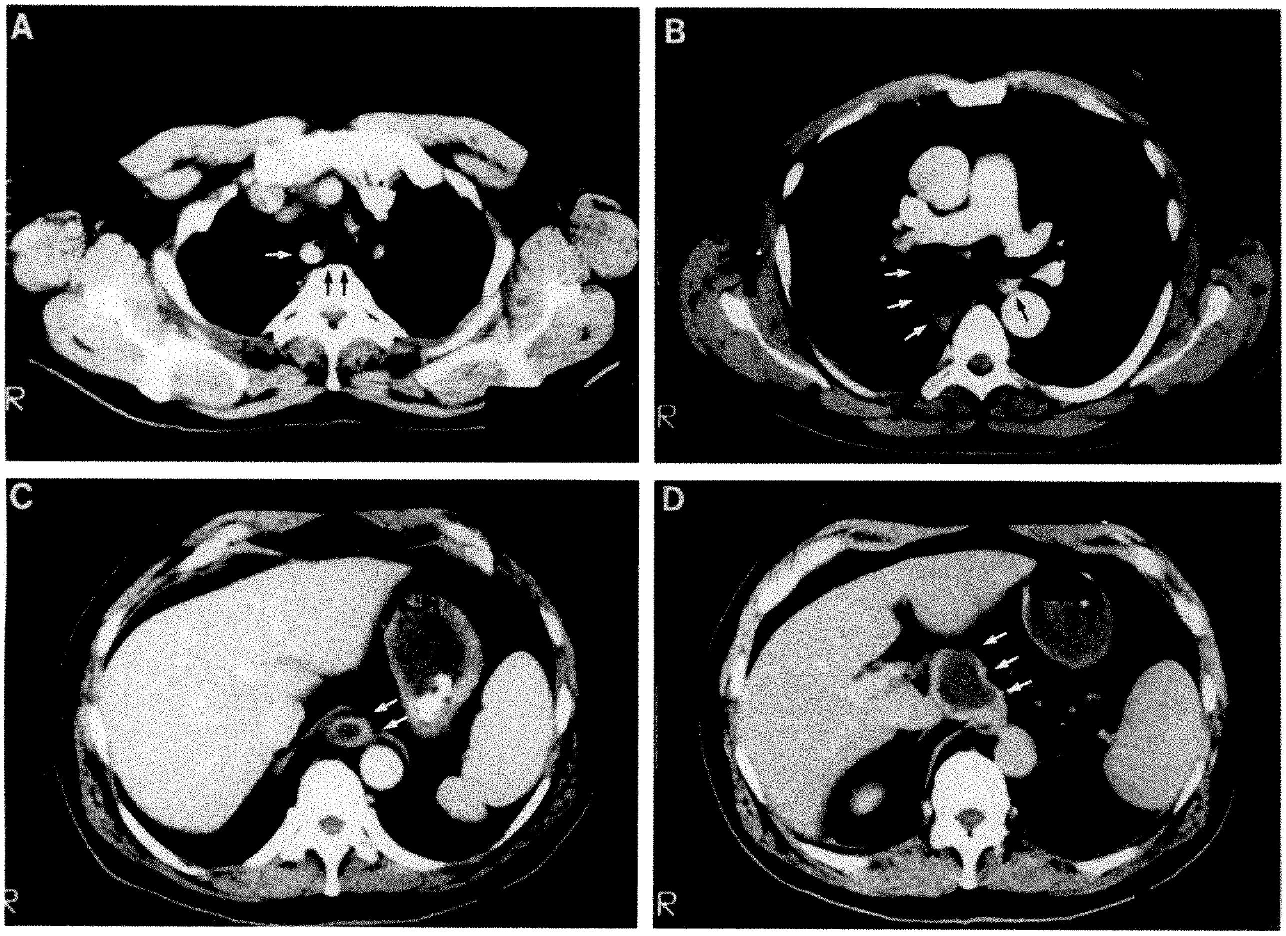

Fig 2. Computed tomographic images outlining the extent of the duplication in the chest and the abdomen. In the upper thorax (A), the air-containing duplication (black arrows) *arises to the left of the esophagus* (white arrow). *In the midthorax (B), the duplication* (white arrows) *is larger (5 cm), contains an air fluid level, and is located to the right of the esophagus* (black arrow). *The duplication narrows at the level of the diaphragmatic crura* (white arrows, *C) and enters the abdomen through a separate hiatus. Posterior to the lobe of the liver (D) the abdominal portion of the duplication becomes larger (5 cm) and is completely fluid filled with a soft tissue rim* (white arrows).

structure that appeared to be in continuity with the intraabdominal cystic structure. Barium study of the esophagus and stomach were normal. A pouch extended off the medial wall of the second portion of the duodenum (Fig 3) but did not fill the epigastric cystic structure. Endoscopic assessment of the esophagus and stomach was normal. In the duodenum, the ampulla was felt to be slightly more posterior than usual and an out-pouching of mucosa was seen. When the mucosa was invaginated and filled with contrast medium, a defect similar to that on the upper gastrointestinal study was seen. A normal pancreatic duct was visualized.

Contrast medium studies of the small and large bowels and colonoscopy were normal. Celiac, superior mesenteric, and inferior mesenteric arteriograms were normal showing no neovascularity, varicosities, or arteriovenous malformations. A Meckel scan was negative for ectopic gastric mucosa either in the chest or the abdomen.

It was assumed that the patient had a complete foregut duplication with intermittent hemorrhage into the duplication. Right posterolateral thoracotomy was performed. The esophageal portion from thoracic inlet to diaphragmatic hiatus was excised first. Cephalad, the duplication was ligated as it narrowed to a 0.5 cm diameter at the thoracic inlet. Distally, the lesion was dissected from its separate hiatus and transected at that level. The diaphragmatic defect and thoracotomy were then closed. An upper midline laparotomy was performed, and the abdominal portion was excised after its identification in the retroperitoneum. The duplication was opened and found to be lined with hemorrhagic, ulcerated mucosa. A 3-mm biliary probe was passed through a small distal tract through the head of the pancreas and into the second portion of duodenum. The duplication was dissected down to the level of this tract and divided distally with a gastrointestinal anastomosis stapler. No abnormal vascular supply was encountered.

The esophageal component contained normal squamous epithelium and muscular walls. The abdominal component had normal gastric mucosa with areas of ulceration and hemorrhage.

Postoperatively, the patient did well and was dis-

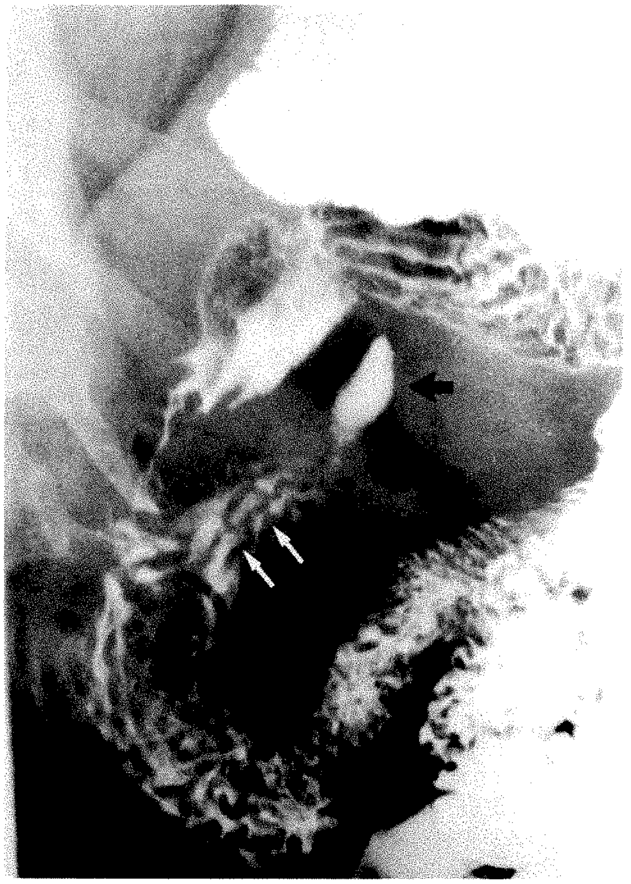

Fig 3. Barium fills the distal aspect of the duplication in a retrograde fashion (black arrow)*. Mucosal folds* (white arrows) *are identified where the duplication inserts into the second portion of the duodenum.*

charged on postoperative day 10. His hemoglobin level has remained normal 1 year after resection.

Comment

This report presents a case of a complete foregut duplication with the normal, mature mucosa belonging to the appropriate structure.

Alimentary tract duplications are unusual even in the pediatric population. Only 10% to 15% of alimentary tract duplications involve the esophagus, with approximately 60% being in the distal portion [2]. The majority of alimentary tract duplications are first seen in the pediatric age group with symptoms of dyspnea, dysphagia, recurrent pneumonia, and failure to thrive. Approximately one third of esophageal duplications are identified in adults, and they are frequently asymptomatic.

Duplication of the esophagus is a congenital anomaly that may begin to develop as early as the fourth week of gestation. As the foregut epithelium develops, it elongates, develops a lumen, and undergoes dextro-rotation. Thus, the majority of esophageal duplications occur distally and on the right.

In a recent review of the literature [2], only six tubular duplications of 44 esophageal duplications were identified. They varied in length from 2 to 36 cm in length, and no mention was made of continuity with a duplicated stomach.

In another large review of alimentary tract duplications [3], 22% were intrathoracic, and all were cystic rather than tubular. Eight percent had cystic gastric duplications along the greater curvature and did not communicate with the stomach. Three percent had thoracoabdominal duplication associated with thoracic vertebral anomalies. There were no recorded esophageal-gastric duplications.

Other rare thoracoabdominal duplications have been identified [3] as arising from various portions of small or large bowel and extending into the thorax through a separate diaphragmatic hiatus. All alimentary duplications extending into the thorax contain alimentary tract mucosa with the most common being gastric mucosa. The majority of these duplications are closed, and less than 10% communicate with the normal alimentary tract. None have been identified to include a normal stomach with gastric mucosa in continuity with an esophagus that had normal squamous epithelium.

In the pediatric literature, ulceration of a thoracic esophageal duplication lined with gastric mucosa may occur with resultant hemorrhage. Although our patient is not within the pediatric age group, his symptoms had been present, by his estimation, since he was 18 years old. Recommended therapy for symptomatic lesions has been surgical excision. Initial attempts at marsupialization resulted in many complications making complete excision of the duplication a more favored option [3, 4]. Operative morbidity and mortality are low, and recurrent symptoms have not been reported. Complete operative excision of alimentary duplications is the management of choice.

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Acute Symptoms Due to a Huge Duplication Cyst Ruptured Into the Esophagus

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A 36-year-old housewife complained of a tight feeling in the pharynx with increasing dysphagia, dyspnea, and mild fever. Chest roentgenogram was interpreted as a cystic mass in the middle mediastinum. Computed tomography showed a cystic mass compressing the carina and the esophagus. Ten days after onset, symptoms were suddenly relieved followed by a tarry stool. The chest mass shadow decreased. Esophagofiberscopy showed two fistulas communicating with a cyst that had two chambers. Thoracotomy performed 40 days after onset showed a true duplication of the esophagus with rupture into the esophagus. This is a rare case in which it was possible to observe the sequence of events of a ruptured intramural duplication cyst by means of chest roentgenography, computed tomography, esophagofiberscopy, and cystogram.

(Ann Thorac Surg 1990;50:309–11)

Most patients with esophageal duplication have no symptoms. However, when the cyst is huge or when there is bleeding or inflammation, dysphagia or chest pain may occur. Recently, we encountered a patient with acute and dramatic symptoms due to a huge duplication cyst that ruptured into the esophagus during the period of observation.

A 36-year-old housewife complained of a tight feeling in the pharynx on October 10, 1986. Dysphagia, dyspnea, and fever up to 38°C gradually developed during the following 7 days. Chest roentgenogram (Fig 1) taken 4 days after onset showed an 8 × 8-cm mass shadow in the middle of the mediastinum. Severe deviation of the esophagus was revealed by esophagogram. The computed tomogram at this time showed a bilateral pleural effusion and a huge cystic mass displacing the carina anterolaterally and the esophagus to the right side (Fig 2). Ten days after onset, symptoms were suddenly relieved followed by a tarry stool.

At the time of hospital admission (10 days after onset), the chest roentgenogram showed that the mass shadow in the mediastinum had decreased to 4 × 4 cm (Fig 3). At this time, the computed tomogram did not show the deviation of the carina and of the esophagus. Esophagofiberscopy (Fig 4A) showed two fistulas (7 mm in diameter each) on the left side of the esophageal wall 33 cm from the incisor teeth. The cyst (Fig 4B) demonstrated two chambers

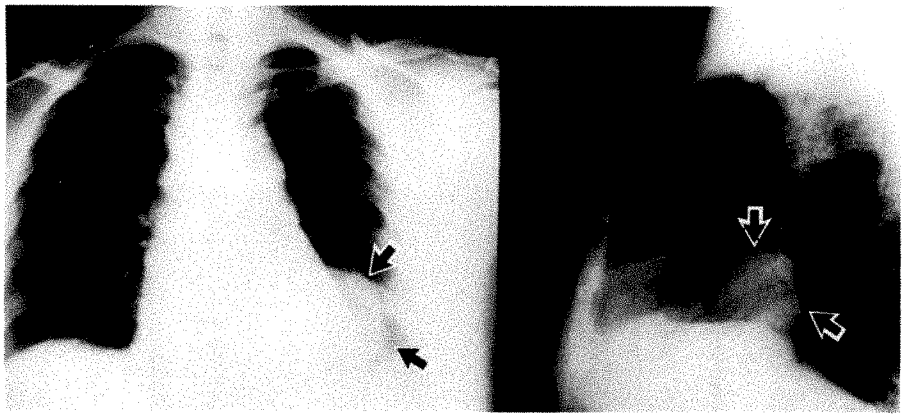

Fig 1. Chest roentgenograms taken 4 days after onset show a mass shadow 8 × 8 cm in diameter in the middle mediastinum.

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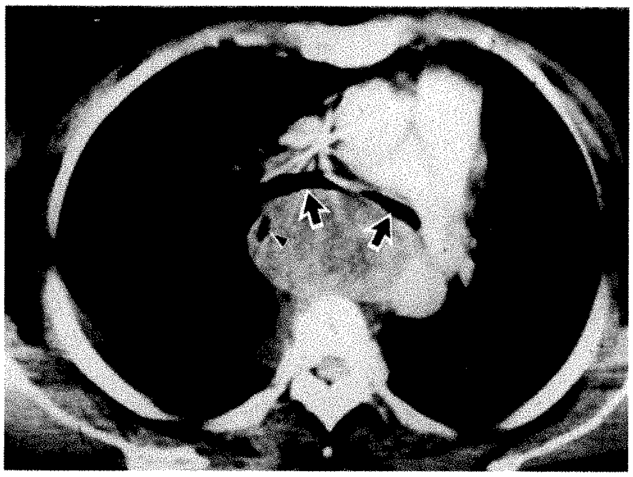


Fig 2. Computed tomography shows a cystic mass displacing the carina anterolaterally (arrows) *and the esophagus to the right side* (triangle).

separated from each other by a septum and containing viscous fluid. Cystogram (Fig 5) clearly demonstrated the cysts and the septum, and roentgenogram showed no vertebral anomaly.

Operation was performed 40 days after onset. Findings were consistent with those assumed before operation: the cyst extended from the level of the carina to 7 cm below and was adherent to the esophagus with a 4-cm base. It was covered with the muscle layers typical of the esophagus. After resection of the cyst, the fistulas were closed with interrupted sutures of 4-0 Vicryl, and the muscle layers were closed with 2-2 silk sutures. Histologically, the cyst wall consisted of stratified squamous epithelium and ciliated cuboidal epithelium with two layers of smooth muscle and nervous plexus. There was no cartilage; thus, an esophageal cyst (true duplication) was diagnosed. The patient had an uneventful course and was discharged from the hospital on the 26th postoperative day.

Comment

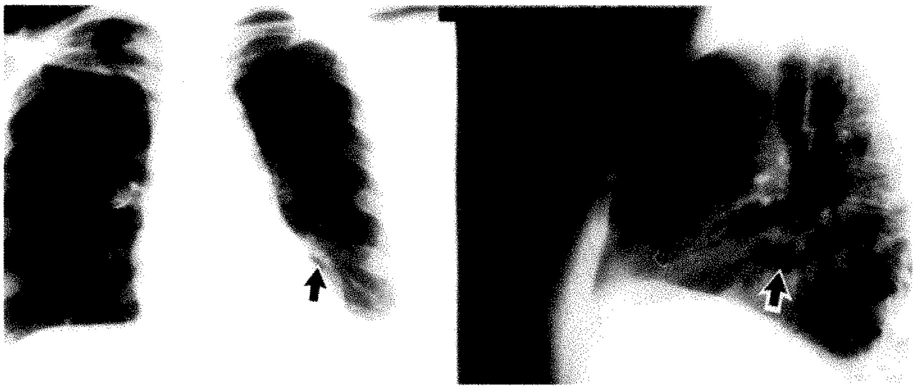
Rubash and co-workers [1] reported that the incidence of esophageal duplication cysts was 1.0% of 186 mediastinal tumors. In our institute, only 2 of 580 resected mediastinal tumors were esophageal duplications.

Embryologically, cystic intrathoracic derivatives of the foregut are classified into 3 categories: bronchogenic cyst, intramural esophageal cyst (true duplication), and enteric cyst resulting from the split notochord syndrome [2]. In our patient, the cyst was covered with muscle layers typical of the esophagus. There was neither cartilage in the cyst wall nor vertebral anomaly. Thus, we regarded our case as a true duplication cyst.

Acute symptoms such as dyspnea, dysphagia, and pneumonia are common in infants with huge duplications of the esophagus [3, 4]. On the other hand, asymptomatic duplication is usual in adult patients [5], although gastrointestinal symptoms such as dysphagia, nausea, vomiting, weight loss, and anorexia have been reported [6, 7]. Gatzinsky and colleagues [8] reported an adult patient with duplication cyst whose symptoms of severe retrosternal pain and dysphagia due to intracystic bleeding suddenly disappeared when the cyst ruptured into the mediastinum.

In our patient, sudden onset of symptoms might have been due to acute enlargement of the cyst from bleeding or inflammation; however, neither was demonstrated [7, 8]. Roentgenographic and computed tomographic findings of a remarkable displacement of the carina and the esophagus by the cyst explain these symptoms. After melena was observed, the symptoms suddenly subsided,

Fig 3. Chest roentgenogram taken at admission, when the patient had no symptoms, shows the mass size decreased to 4 × 4 cm (arrow).



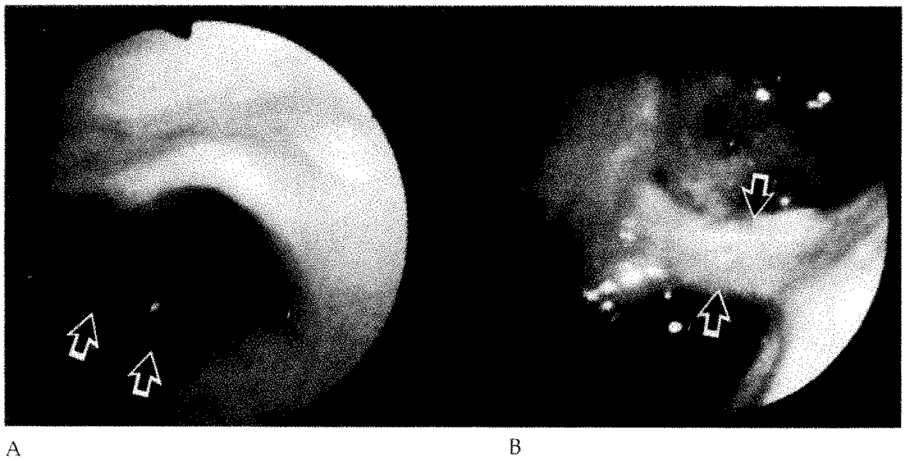


Fig 4. (A) Esophagofiberscopy shows two fistulas, 7 mm in diameter each, on the left side of the esophagus (arrows). (B) The cyst had two chambers with a septum (arrows).

which was interpreted as rupture of the cyst into the esophagus.

Thus, in this rare case, it was possible to observe, by means of chest roentgenography, computed tomography, esophagofiberscopy, and cystogram, the sequence of a rupture of an intramural duplication cyst.

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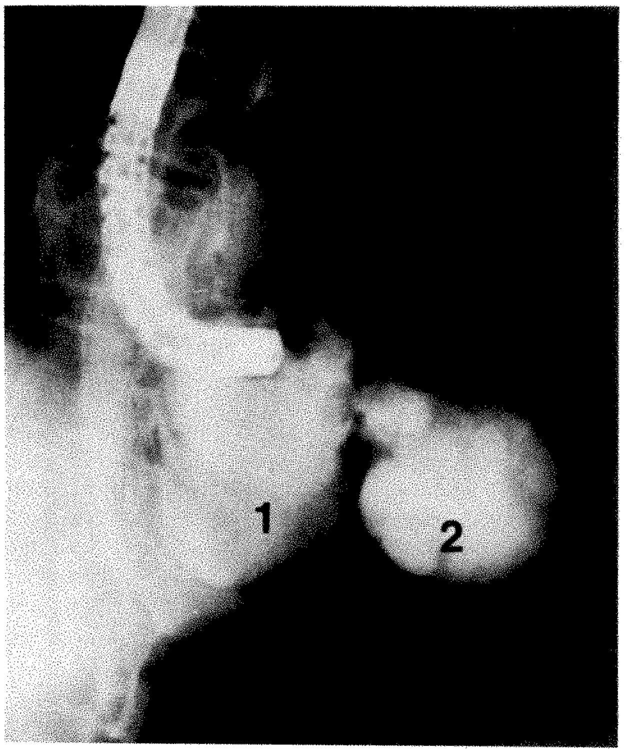

Fig 5. Cystogram shows a cyst with two chambers in the lower part of the esophagus (1 and 2).

Bilateral Pulmonary Nodules Caused by *Dirofilaria immitis*

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The unusual case of bilateral lung nodules caused by *Dirofilaria immitis* in a 44-year-old woman is presented. A brief discussion of the life cycle of this parasite, the clinical and epidemiological features of human infestation, and the roentgenographic and laboratory findings is given.

(Ann Thorac Surg 1990;50:312–3)

A pulmonary lesion caused by *Dirofilaria immitis* is no stranger to the low-lying areas of South Carolina. In 1975, 5 cases were reported from the Charleston area by Prioleau and co-workers [1]. This was the largest series in the English-language literature at that time. Since then, there have been more reports of single lesions, and in 1982, Ciferri [2] published a collective review of 60 cases. In that review, South Carolina ranked third behind Florida and Texas in the number of cases reported. Our group has treated several additional cases during the past few years. The unusual occurrence of bilateral pulmonary lesions caused by *D immitis* warrants the addition of this case to those previously recorded.

It is not surprising to find this case in coastal South Carolina. The diagnosis was suspected preoperatively. All of the criteria exist here for human infestation with *D immitis*. There is a large dog population with a prevalence of infected carriers. The mosquito population during the warm months can be awesome. It seems to be the one entity hurricane Hugo did not damage. The weather and waterways furnish a mecca for fishing and other outdoor activities, thus exposing the population to *Dirofilaria* infestation.

A 44-year-old woman was found to have bilateral pulmonary densities on a routine chest roentgenogram (Fig 1). She was a moderate smoker for 25 years. Her past health had been good, and she had no prior pulmonary symptoms. A computed tomographic scan of the chest confirmed discrete rounded densities in both lower lungs. A needle biopsy was done on one of these. The pattern described was suggestive of a *Dirofilaria*-related granuloma but the parasite was not seen. The pathologist commented that bilateral dirofilariasis is relatively rare. On February 14, 1989, bilateral lung lesions were excised through a median sternotomy incision. Both lesions showed a necrotizing pulmonary process with inflammatory, lymphoid, and giant cell reaction and with microscopic round worms consistent with *D immitis*. The patient had a satisfactory recovery.

Comment

Dirofilaria immitis is a common filarial heart parasite found in dogs in large endemic areas, especially along the eastern seaboard. Humans are unsuitable hosts resulting in death of the larval form, which embolizes from the right side of the heart to a terminal branch of the pulmonary artery, causing a small infarct. Dashiell [3] reported this entity for the first time in 1961.

Bilateral pulmonary lesions and multiple unilateral lesions are rare. Awe and associates [4] reported the first case of bilateral pulmonary nodules caused by *D immitis* removed through median sternotomy in 1975. Beskin and Colvin [5] reported a case of bilateral nodules, but only one side was removed and confirmed. The nodule in the opposite lung remained unchanged for 19 months. Lum [6] reported three proven lesions in the right lower lobe of a patient who died after myocardial revascularization.

Life Cycle

Dirofilaria immitis and its life cycle are described in detail by Adkins and Dao [7] and by Lau and Pierson [8]. In brief, the microfilariae are ingested by the mosquito when an infected dog is bitten. These molt in the mosquito and can be injected into humans through mosquito bites. Most die in the subcutaneous tissue, but uncommonly some microfilariae develop further and move to the pulmonary circulatory system. Because of human host resistance, maturity is not reached. They eventually die and embolize to a branch of the pulmonary artery producing a small ischemic infarct.

Clinical and Epidemiological Features

In Ciferri's collective review [2], the male-to-female ratio was 2:1 with an age range of 28 to 77 years. Symptoms occurred in only 41% of patients reported and consisted of chest discomfort, malaise, low-grade fever, cough, and infrequently hemoptysis.

Roentgenographic and Laboratory Findings

The usual appearance of *Dirofilaria* in chest roentgenograms is that of a 2- to 3-cm rounded density in the periphery of the lung containing no calcium. Unlike the usual pyramidal configuration of a pulmonary infarct, a rounded density is seen, which is thought to be due to the

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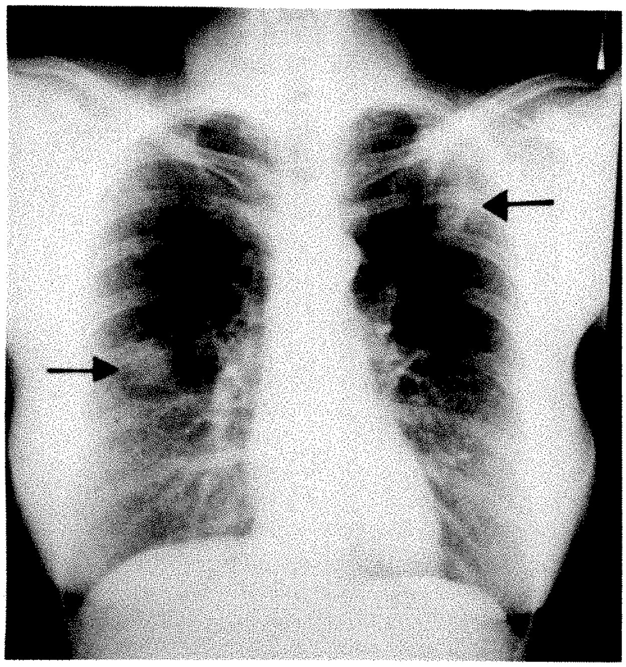

Fig 1. *Bilateral pulmonary lesions.*

local reaction of the lung to the foreign protein material. The interval between a chest roentgenogram negative for this density and one showing this density varies. Kochar [9] reported 1 patient with a negative chest roentgenogram 2 months before the finding of a nodule, and 2 patients whose roentgenographic findings converted from negative to positive in 3 weeks. The initial radiologic change in these 2 patients was an infiltrate with a pleural effusion. Discrete nodules followed resolution of the infiltrate, supporting the concept that local pneumonitis results in a rounded density rather than the usual pyramidal density of an infarct.

Peripheral eosinophilia is seen infrequently, probably because of the small amount of antigen produced by one or several worms. Serologic tests thus far have failed to be specific enough for definitive diagnosis. Fine needle biopsies, likewise, are not specific enough to rule out carcinoma. Therefore, surgical excision is usually required to confirm the diagnosis consistent with the usual indications for lung nodules.

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A Fiber-Optic Retractor for Harvesting the Internal Mammary Artery

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A retractor for exposure and dissection of the internal mammary artery incorporating a fiber-optic transillumination system is presented. The device, which can be converted to a standard sternal retractor, has also proved valuable in improving illumination during procedures on the mitral valve and in facilitating dissection of fibrous adhesions from the anterior surface of the heart at reoperation.

(Ann Thorac Surg 1990;50:314–5)

Steady position, optimal exposure, and good light are essential during harvesting of the internal mammary artery. Although the first two factors can be achieved with recently introduced retractors, good illumination of the mammary artery bed remains a problem [1–3].

We have developed a retractor incorporating a new fiber-optic transillumination system in which the fibers have been bent at 90 degrees into a cylinder-shaped device to produce a longitudinal light window. When positioned on the retractor blade opposite the mammary

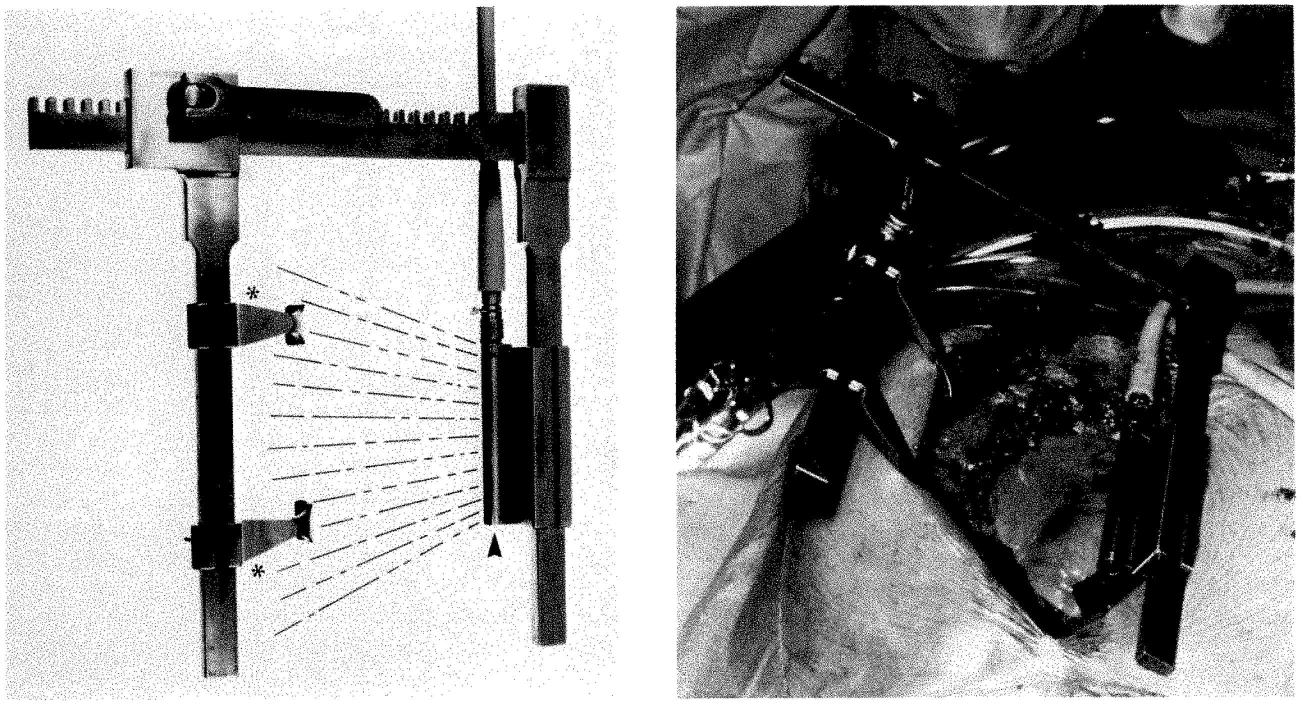

*Fig 1. (A) Lateral view of the retractor with schematic representation of the light generated by the transillumination system (*angled blades; ▲ fibre-optic illuminated unit). (B) Lateral view of the retractor in position. The side of the internal mammary artery is elevated by the angled blades while the opposite side is slightly depressed.*

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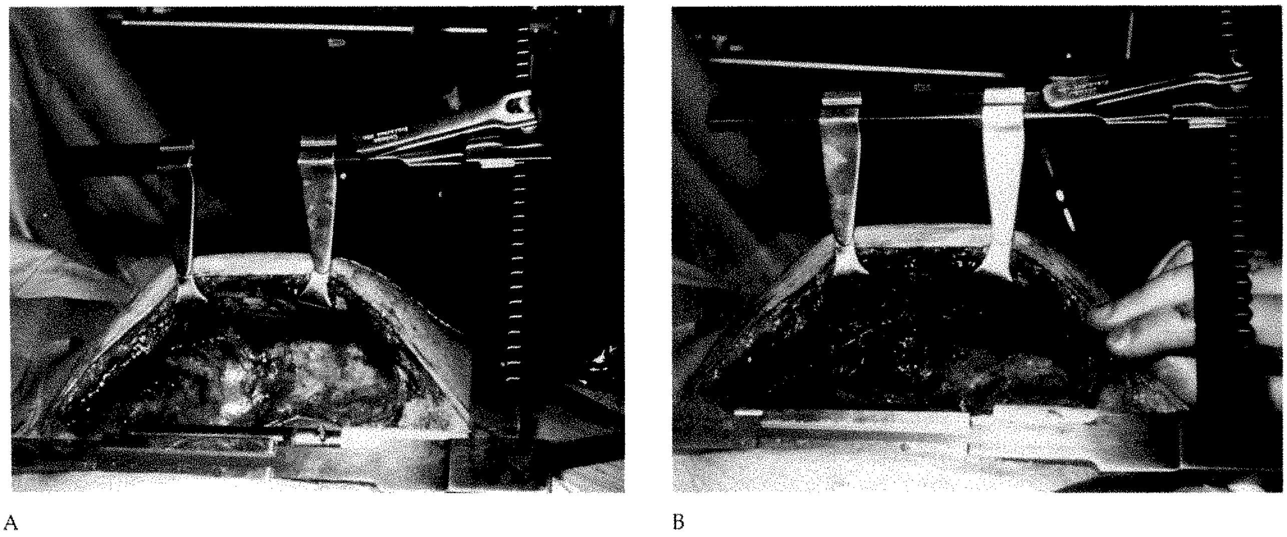

Fig 2. (A) Frontal view of the retractor in position with schematic representation of the anatomical course of the internal mammary artery. (B) Dissected internal mammary artery.

artery to be harvested, the device will illuminate the mammary artery bed without any need for additional light.

Material and Methods

The instrument is based on a lightweight stainless steel sternal retractor with conventional rack-winding handle that can be mounted on either side of the retractor body to enable harvesting of either left or right internal mammary artery. Two angled blades can be mounted at any position along the blade-receiving area on the side of the internal mammary artery to be dissected (Fig 1A). A knurled nut locks the blade to prevent slipping. The illuminated sternal blade is contoured to cradle the sternal edge. The smooth inner surface of the blade allows it to rotate around the sternal edge as a fulcrum without damaging it during the lifting motion of the retractor initiated by the angled blades on the opposite side. The fiber-optic illuminated unit is a unique continuous 10 cm × 1 mm fiber-optic port that delivers a bright light directly onto the internal mammary artery bed (Fig 1A). The fiber-optic component, which slides into the grooved sternal blade, is capable of being inserted from either end of the blade to enable the fiber-optic cable to fall away from the retractor from the most convenient side. The angle of illumination may be easily changed by rotating the housing of the fiber-optic unit allowing optimum illumination, as the elastic deformation of the chest wall differs from patient to patient.

With the two angled blades in place on the side of the internal mammary artery to be exposed and with the illuminated blade on the opposite side, the surgeon will wind open the retractor arms. The combination of the angle of the blades and the mechanical advantage of the opposing force dictate that the side of the internal mammary artery will elevate and rotate outward, while the other side will be slightly depressed (Fig 1B). The resulting space will enable the surgeon to identify, expose, and dissect the internal mammary artery under excellent illumination yet only using the predictable elastic deformation of the chest wall (Fig 2). The retractor can be removed and replaced easily at any stage of the procedure. Once the internal mammary artery has been dissected, the angled blades can be replaced by a standard sternal blade similar in shape to the illuminated blade and the instrument used for normal sternal retraction. All components of the retractor can be autoclaved at 134°C.

Comment

The retractor has been used routinely for the last year and has allowed quick, easy, and accurate harvesting of the internal mammary artery. It has improved illumination during procedures on the mitral valve and has also facilitated exposure of the anterior surface of the heart during dissection of fibrous adhesions at reoperation.

We thank Mr Nigel Watkin of Codman Ltd UK for assistance in the design, development, and manufacture of the retractor prototype.

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Hemostatic Technique for Internal Mammary Artery Anastomotic Bleeding

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When internal mammary artery is used for myocardial revascularization, a not uncommon occurrence is intraoperative bleeding from the internal mammary artery to coronary artery anastomosis. The conventional method of hemostasis of placing additional sutures across the suture line may produce anastomotic stenosis or may aggravate the bleeding by producing tears, especially as these additional sutures are placed on a beating heart. We describe a simple technique by which hemostasis can be achieved without the risk of anastomotic stenosis or aggravation of the bleeding, as it avoids placing sutures over the anastomotic suture line.

(Ann Thorac Surg 1990;50:316–7)

Internal mammary artery is accepted as the best conduit for myocardial revascularization. Intraoperative bleeding from the anastomotic suture line is not an uncommon occurrence. The conventional method of hemostasis of placing additional sutures at the bleeding points, across the suture line, may produce anastomotic stenosis or may aggravate the bleeding by producing tears (as the tissues may be friable, altered by disease) as the sutures are taken on a beating heart.

It is our experience that hemostasis can be achieved by tightening the anastomotic suture line a little bit more as the sutures are placed precisely in the first instance. Additional sutures across the suture line are best avoided unless absolutely mandatory.

The hemostatic technique described here does away with the need to place additional sutures across the suture line. In this technique, after the suture line is tightened by pulling the Prolene loop, the knots fall on the suture line. It is simple, safe, effective, and reproducible.

Technique

The left internal mammary artery is anastomosed to a coronary vessel in an end-to-side fashion by continuous suturing technique, with adequate light and adequate magnification (with prism loops of 4.5 magnification) using 7-0 Prolene (Johnson & Johnson) suture on a BV-1 needle.

When there is bleeding from the anastomic suture line, a loop of the continuous suture is raised with a hook adjacent to the bleeding point (Figs 1A–D). If there is bleeding from the toe of the anastomosis, the loop is raised at the toe and shifted to the lateral border (Fig 2), and the maneuver is applied. The same is true for bleeding at the heel of the anastomosis.

A piece of 7-0 Prolene suture is passed through the loop and the two ends are held in a hemostat (Fig 1E). A 7-0 Prolene epicardial stitch is placed adjacent to the raised loop (Fig 3A) and tied. One end is held in a hemostat (Fig

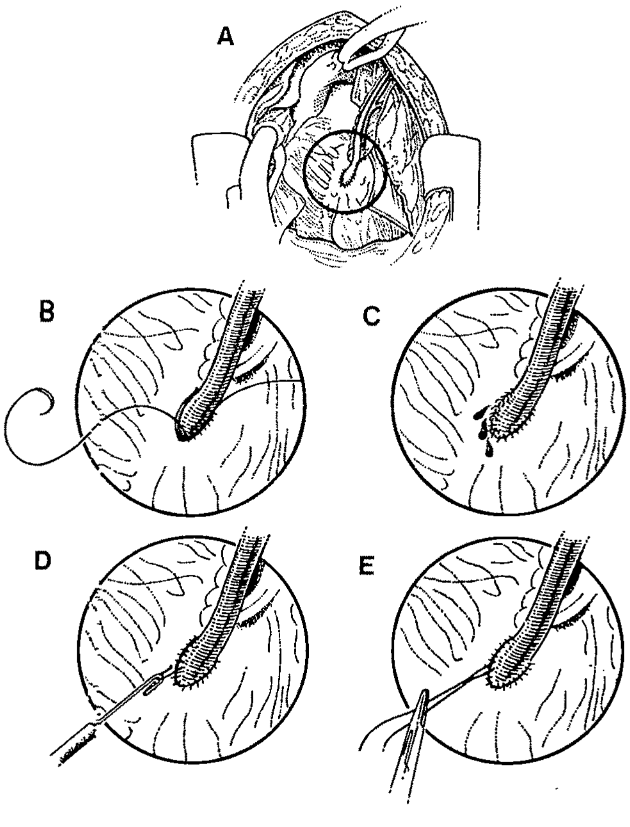

Fig 1. *(A) The internal mammary artery is anastomosed to the coronary vessel. After the anastomosis is completed (B), if bleeding remains (C), a loop of the suture is raised (D) and a piece of 7-0 suture material is passed through (E).*

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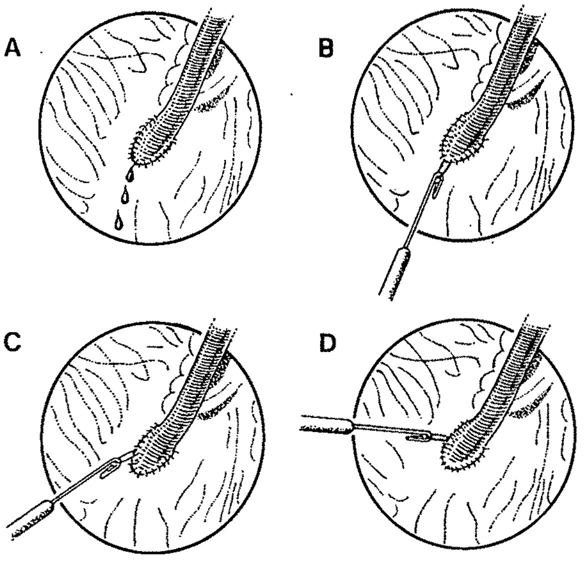

Fig 2. If there is bleeding from the toe of the anastomosis (A), the loop is raised at the toe (B) and shifted to the lateral border (C, D).

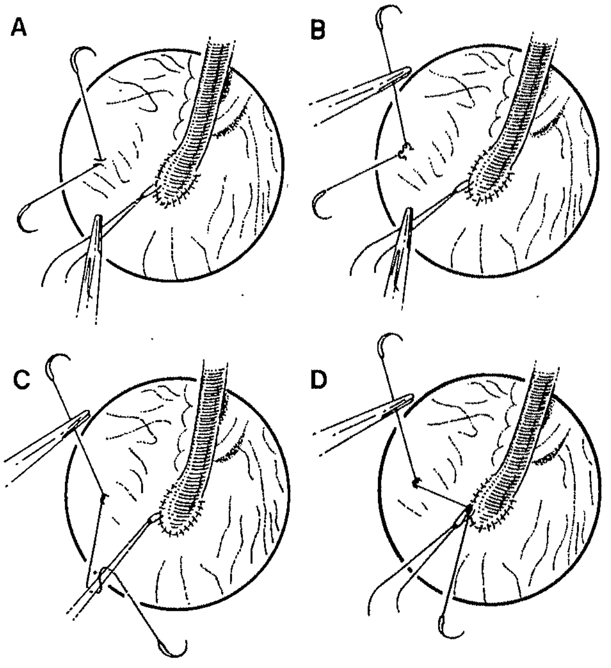

Fig 3. (A) An epicardial stitch is placed adjacent to the raised loop and tied. One end is held in a hemostat (B) and the other end is tied to the piece of suture passed through the loop (C) in such a way that the knots fall at the base of the loop (D).

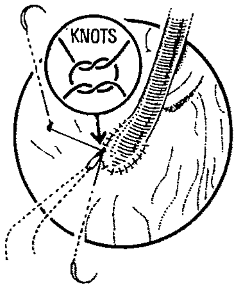

Fig 4. The final knots fall at the base of the loop, the extra piece of suture material is removed, and the ends of the sutures are cut.

3B) and the other end (not the end held in the hemostat) is tied to the piece of 7-0 suture passed through the loop (Fig 3C) in such a way that the knots fall at the base of the loop (Fig 3D). This fixes the loop on the suture line and tightens the anastomosis so that the final knots will be at the base of the loop. The 7-0 Prolene piece passed through the loop is removed, and the ends of the sutures are cut (Fig 4).

Comment

This technique does away with the anxiety of placing additional sutures across the suture line on a beating heart and does not produce anastomotic stenosis or aggravate the bleeding by producing tears when the tissues are altered by disease. We have not experienced any break of a 7-0 Prolene suture with another piece of 7-0 Prolene suture as the traction string. This technique is also better than raising the loop and fixing it onto the adjoining epicardium (Fig 5), in which the knots fall away from the suture line and also cause traction distortion of the anastomotic suture line.

This technique can be applied to other distal anastomoses of reversed saphenous vein grafts, to proximal aortic anastomoses, to a loose loop left out of a vascular anastomosis, and in fact to any bleeding suture line. We recommend this technique as it is simple, safe, effective, and reproducible.

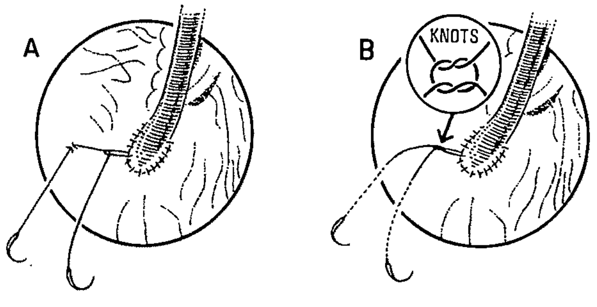

Fig 5. When the technique in which the loop is raised and fixed onto the adjoining epicardium (A) is used, the knots fall away from the suture line (B).

Biatrial Transseptal Approach in Case of Difficult Exposure to the Mitral Valve

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The biatrial transseptal approach according to the Dubost technique provides an excellent exposure to the mitral valve. Over a 5-year period (1984 to 1989) we used this approach in 210 patients. We believe that this incision is indicated in the following situations: reoperation on the mitral valve and acute mitral insufficiency with little enlargement of the left atrium.

(Ann Thorac Surg 1990;50:318–9)

The routine left atriotomy through the interatrial groove does not constantly provide optimal exposure to the mitral valve that would allow performance of valve reconstruction or replacement in good conditions. In 1966, Dubost and associates [1] described the biatrial transseptal approach, which offers an excellent exposure to the mitral valve. We have been using this incision since, and at present it constitutes our incision of choice in two situations. (1) During reoperation on the mitral valve, the mitral apparatus is usually fixed in a horizontal plane and mobilization of the mitral annulus is severely restricted unless the left ventricle has been completely freed of pericardial adhesions. (2) In cases of acute or subacute mitral insufficiency there is frequently little dilatation of the left atrium; therefore, difficult exposure to the mitral valve may be expected.

Technique

Extracorporeal circulation is instituted in a routine fashion, and double venous cannulation and control of both vena cavae are required. The right atrium is opened by an incision running from the superior pulmonary vein between the two venous cannulas and around the insertion site of the inferior venous cannula (Fig 1). In cases of extensive pericardial adhesions with invisible atrioventricular groove, one must be cautious not to injure the right coronary artery.

The interatrial septum is then opened at the level of the fossa ovalis perpendicular to the tricuspid valve. This incision is prolonged on the right superior pulmonary vein (Fig 2). The septum is then incised according to a line running 2 cm behind the coronary sinus (to avoid the conduction pathways), parallel to the tricuspid valve, and ending at the floor of the atrium (Fig 3). Using a single retractor, an excellent exposure to the mitral valve may be obtained through this approach (Fig 4). Replacement of a dysfunctioning prosthesis as well as complex valve reconstruction can be performed in good conditions.

At the end of the operation, the septal and atrial incisions are closed in a routine fashion with a running suture. One may introduce a right atrial catheter into the suture line of the septal incision to obtain postoperative left atrial pressure monitoring. The junction between the superior pulmonary vein and the septum on one hand and the right atrial wall on the other must be closed carefully to prevent bleeding complications and secondary left-to-right shunting.

Comment

The approach to the mitral valve through the right atrium and the interatrial septum has been variously described in the past [2, 3]. We have had extensive experience with the biatrial transseptal approach for valvar operations according to Dubost's technique [1, 4]. Over the past 5 years (1984 to 1989), this approach has been used in 210 patients at our institution. It was used either in cases of redo cardiac operations (97 second, 28 third, 7 fourth, and 3 fifth sternotomies) or in cases of acute mitral insufficiency with little enlargement of the left atrial cavity (n = 66). In rare instances, this incision was used for combined mitral and tricuspid operations (n = 9).

Injury to the right coronary artery when opening the right atrial cavity was observed in 2 patients with exten-

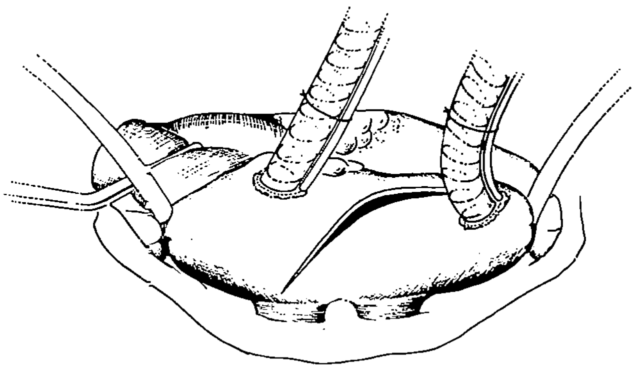

Fig 1. Right atrial incision extending from the right superior pulmonary vein between both venous cannulas and around the insertion site of the inferior venous cannula.

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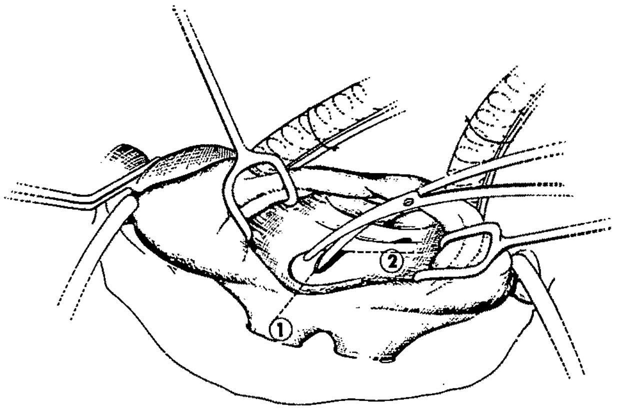

Fig 2. Septal incision: the interatrial septum is opened at the level of the fossa ovalis. The incision forms a 90-degree angle reaching the superior pulmonary vein laterally (1) and the atrial floor inferiorly (2).

sive pericardial adhesions, but immediate repair was performed with a good outcome. A left-to-right shunt secondary to inappropriate closure of the septal incision was noted in 1 patient requiring reoperation.

To establish the exact incidence of conduction system disturbances induced by the biatrial transseptal approach, we reviewed a select group of patients who underwent biatrial transseptal approach for isolated mitral valve repair operated on for the first time (n = 66). Temporary electrosystolic stimulation was required in 21 of these patients during the postoperative course (mainly because of a slow nodal rythm) and was discontinued in most patients within 48 hours or after a maximal time lapse of 2 weeks. No patient required permanent pacemaker insertion. Episodes of atrial fibrillation (n = 12) and atrioventricular block of the first degree (n = 8) were also noted.

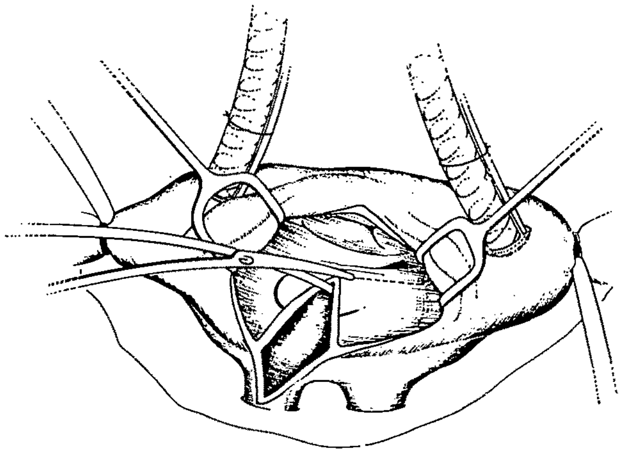

Fig 3. After the septal incision toward the superior pulmonary vein, the septum is cut according to a line (dotted) running 2 cm behind the coronary sinus and parallel to the tricuspid valve.

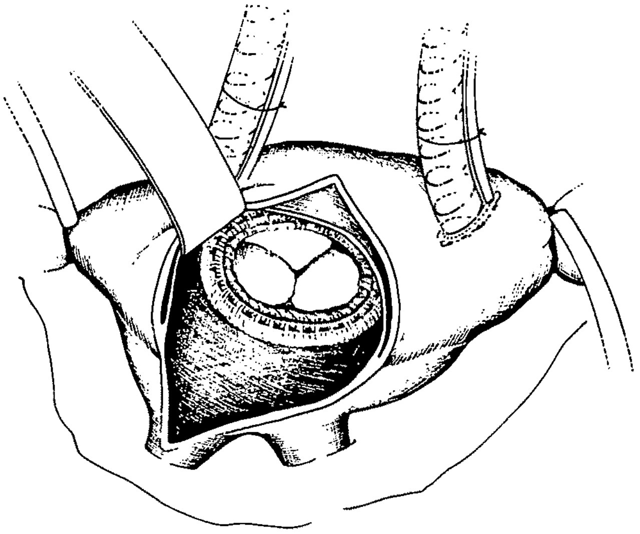

Fig 4. Using a single retractor, an excellent exposure to the mitral valve is obtained.

Because of the higher incidence of conduction system disturbances, we believe that the biatrial transseptal approach should be restricted to patients in whom a poor exposure to the mitral valve is expected. We do not consider the need for a combined mitral and tricuspid operation an indication for this incision provided that a selective approach of both atria is feasible.

In conclusion, the biatrial transseptal incision is the best approach for mitral valve repair/replacement to obtain an optimal exposure to the mitral valve in difficult cases. (1) During reoperation on the mitral valve, the presence of pericardial adhesions imposes a horizontal plane to the mitral orifice (especially if an aortic prosthesis is already in place). Mobilization of these adhesions includes a risk of diffuse postoperative bleeding and increases the risk of left ventricular rupture in case mitral valve replacement is performed. (2) In cases of acute mitral insufficiency with little enlargement of the left atrium, a complex mitral valve reconstruction may be required (acute endocarditis, degenerative lesions) and optimal exposure to the mitral leaflets and to the subvalvar mitral apparatus must be obtained.

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Use of the Allograft Aortic Valved Conduit

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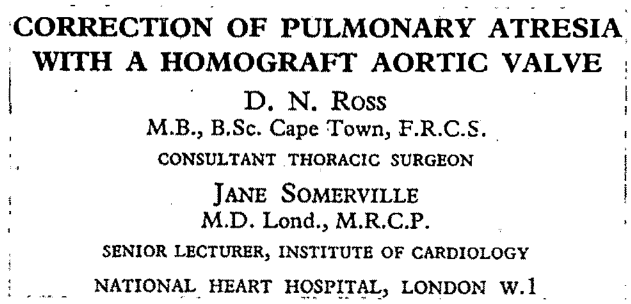
Although the clinical use of the subcoronary free-sewn allograft aortic valve was first described by Ross and Barratt-Boyes independently in 1962, the use of an allograft valved conduit for right ventricular outflow tract reconstruction in congenital cardiac surgery was not considered until February 14, 1966. With the description of this successful application by Ross and Somerville, the corrections of many previously inoperable cardiac lesions soon followed.

(Ann Thorac Surg 1990;50:320–2)



CORRECTION OF PULMONARY ATRESIA WITH A HOMOGRAFT AORTIC VALVE

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Before 1966, many congenital cardiac defects with right ventricle to pulmonary artery stenosis or discontinuity (true pulmonary atresias) and large collaterals were deemed uncorrectable or carried a very high operative risk for there was no good way of providing a valved connection when pulmonary hypertension was present. Though others had used direct connection [1], patch reconstructions [2, 3], and nonvalved conduits made from pericardium [4] for repairs of severe tetralogy of Fallot and pulmonary atresia before 1966, right ventricular failure occurred uniformly when pulmonary hypertension was present. Even when the pulmonary artery pressures were low, right ventricular failure secondary to severe pulmonary insufficiency and right ventricular volume overload remained a major problem. Ross and Somerville's [5] case report on the use of an allograft aortic-valved conduit for the reconstruction of the right ventricular outflow tract in an 8-year-old boy with severe tetralogy of Fallot changed this dismal outlook for many children with previously lethal congenital cardiac defects. Ross and Somerville's pioneering effort led the way for the successful repairs of severe tetralogy of Fallot, pulmonary atresia, truncus arteriosus, and transposition of the great arteries with pulmonary stenosis as well as other rarer complex congenital heart lesions.

The future seemed bright for the allograft valved conduit, but 5 years later follow-up reports from several centers in the United States [6–8] indicated a considerable obstruction rate from these allografts. Distortion and kinking at the proximal end of the conduit, calcification of the graft, and procurement difficulties were identified as major problems and interest shifted to Dacron tube grafts with porcine bioprostheses for the repair of these lesions, at least in the United States. However, these xenograft bioprosthetic conduits fared little better over time, and obstruction remained a major problem. It became apparent that the leaflets of the porcine bioprosthesis in the conduit calcified, sometimes in a very short time in children, and that neointimal proliferation proximal to the valve in the conduit as described earlier with the allograft conduits also contributed to the obstruction.

Now the pendulum has swung back to the use of the allograft valved conduit as originally described by Ross and Somerville for several reasons. First, we now know that although the aortic allograft wall calcifies, the valve leaflets do not. Furthermore, the obstruction reported earlier was secondary to neointimal peel formation in a circumferential Dacron tube extension placed proximal to the allograft usually to gain length in complex repairs. Today, circumferential tube extensions are to be avoided if possible. The posterior portion of the proximal end of the allograft is attached directly to the right ventricular outflow tract and only a triangular-shaped hood fashioned from either pericardium or polytetrafluoroethylene is used to complete the connection. Second, the early experience with allografts involved a variety of different preservation and sterilization techniques including freeze drying, gamma irradiation, ethylene oxide, and β-propriolactone. All these methods were very damaging to the allograft tissues. If only "fresh antibiotic-preserved" or cryopreserved valve conduits are used, future results with either of these two groups of allografts likely will be better than those of the composite Dacron xenograft conduit. Third, allografts come in all sizes; xenografts do not, and the intrinsic transvalvar gradient of a given-size allograft is insignificant compared with that of a similar-sized bioprosthesis. Therefore, larger diameter allografts can be placed compared with the bulky xenograft bioprosthesis with its attendant sewing ring. "Adult-sized" allografts can be placed even in very small children, thereby avoiding the question of conduit and valve growth, to which an answer is not available at this time.

Finally, the mode of valve failure is likely different

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between the two valved conduits. Xenografts quite often fail by stenosis secondary to calcification whereas allograft valves fail owing to insufficiency. Stenotic valves will usually have to be replaced with time; however, insufficient valves may not be replaced if the degree of pulmonary hypertension is minimal and the right ventricular performance is good.

Procurement still remains a major problem and neither the aortic allograft nor xenograft conduit is ideal, but recently Mr Ross and his colleagues have taken us one step closer. Though it had been described earlier by Eguichi and Asano [9] (1968) and Seki and associates [10] (1970) in laboratory experiments with dogs, Ross pioneered the clinical use of the allograft pulmonary valve conduit for right ventricular outflow tract reconstruction in 1983 [11–13]. This has virtually doubled the number of allografts available for use while the number of allografts available overall has decreased markedly as the field of heart and heart-lung transplantation has exploded. The pulmonary valve allograft is thinner, it has less transvalvar gradient, and it is easier to work with. The calcification of this allograft is substantially less than that of the aortic allograft conduit, and the pulmonary artery allograft provides a major technical advantage in that repairs can be carried out safely even in children with complex pulmonary anatomy. This is particularly true for cases in which multiple severe stenoses or even discontinuity of the pulmonary arteries are present because the branch pulmonary arteries are harvested with the allograft.

These are all notable advantages compared with either of the conduits used previously. Therefore, in 1990 the pulmonary artery allograft must be considered the conduit of choice for right ventricular outflow tract reconstruction.

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Editor's Note

We asked Mr Ross for his comments on Dr Campbell and Dr Clarke's interesting article.

Mr Ross' Commentary

I was very pleased to read this article by Drs Campbell and Clarke on our use of the homograft valved conduit for right ventricular reconstruction. Having struggled with a number of cases of severe Fallot variants presented for correction by my colleague Dr Somerville, it seemed entirely logical to use the beautifully designed aortic homograft to bridge the gap and use the anterior mitral cusp to fill in the ventriculotomy incision.

Our first case was a true outflow atresia but with confluent pulmonary arteries and like many first attempts went without a hitch. Such was our ignorance of the disease pattern at that time that I reopened the left chest about 10 days postoperatively confident that we had to tie a ductus to control the persistent continuous murmur!

That young man is fit and well 24 years later, but his first operation was at the age of 8 years and at that time we thought he should have an appropriately sized small homograft. Naturally he outgrew this valve, which became stenotic, and it was replaced at age 18 years or 14 years ago. The replacement still serves him well.

As mentioned, early reports were marred by the Mayo Clinic's experience with irradiated valves, which stenosed badly. I reoperated on one of their patients in whom the conduit was so small I mistook it for a coronary artery. We did not have this problem with irradiated valves, so we must assume that the irradiation dosage was excessive.

Also, we have always insisted that the conduit is short and within the line of the right ventricular outflow, whereas a number of earlier conduits were looped in a redundant bridge with consequent kinking and turbulence.

I am surprised and a little ashamed that it took me so long to progress to the next logical step and use the pulmonary homograft rather than the aortic for right-sided reconstruction.

Both Dr Somerville and I retain our enthusiasm for the homograft and proximal extensions of the conduit are with autogenous pericardium.

You will notice that I use the term *homograft* rather than the more recently fashionable *allograft*. The Oxford Dictionary tells me that *allo* (Greek) means "other or different," which in this context is meaningless and applies equally to porcine or pericardial calf valves. *Homo* (Greek) means "similar or the same," and in addition *homo* (Latin) means "man," so on all grounds I believe homograft to be the correct term.

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Paradoxical Hypertension After Repair of Coarctation of the Aorta: A Review of Its Causes

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Correction of a coarctation of the aorta, an apparent simple cause of hypertension, paradoxically can provoke two hypertensive responses, one of which is potentially fatal. The first, limited to the first 24 hours, occurs in nearly one half of the patients. This is likely due to the high set of the carotid baroreceptors. The second, which may be associated with abdominal pain and, in some, with necrosis of the small bowel as a result of severe arteritis confined to arteries arising from the aorta below the coarctation, develops in about one half of the first responders. Norepinephrine excretion greatly increases for several days, whereas angiotensin levels are elevated for 3 to 4 days. The hypertension responds to β-blockers, to arterial smooth muscle relaxants, and to angiotensin converting enzymes. A theory is advanced to explain the second response. It is the adaptation gone awry that ensures adequate flow to exercising muscles below the coarctation, above and beyond that delivered by increasing the systolic pressure. It could be a regionally controlled mechanism similar to the rationing of blood flow in diving mammals.

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That the correction of a coarctation of the aorta, an apparently simple cause of hypertension, can provoke two different hypertensive responses, one of which is life threatening, is unexpected and illogical; thus, the name paradoxical hypertension [1]. The first response occurs immediately and subsides in most patients within 24 hours. The second response, which is more pronounced in diastole, appears within 48 to 72 hours (Fig 1). The striking finding in the second response is the severe acute inflammatory changes that may occur in arteries and arterioles that originate from the aorta below the coarctation [2–4].

In this review, I will give an account of how these postoperative hypertensive events were first recognized and how a therapeutic program was then devised that has virtually eliminated them as serious clinical problems. This will be followed by a review of current thoughts about the physiological adaptations occuring in coarctation that maintain homeostasis. Then I will propose a theory to explain the pathogenesis of the two paradoxical responses based on a disruption of these cardiovascular adaptations.

This story [3] began in 1952 after a 22-year-old man was operated on for coarctation of the aorta. Before operation, the blood pressure in his arms varied from 190 to 215/60 to 0 mm Hg and in his legs, from 140/80 to 0 mm Hg. He had a pronounced aortic valvar insufficiency. In the immediate postoperative period, his blood pressure increased in his arms and legs from 140/80 mm Hg on the first day to 224/94 mm Hg on the third day. At this time, he complained of moderately severe abdominal pain. He died 13 days later during removal of most of the ileum and jejunum for necrosis. At autopsy, severe acute arteritis was found in the arterial system connected to the aorta by the vessels originating from below the coarctation [3]. The changes noted were a disruption of the walls of the vessels associated with fibrinoid necrosis and intense acute inflammatory exudate. The pathologist described the change as resembling periarteritis nodosa. Lober and Lillehei [4] made a similar comparison in their study.

The second patient, a 4-year-old boy, was admitted a little more than a year later. His blood pressure was 150/80 mm Hg in his arms and 90/65 mm Hg in his legs. The coarctation of the aorta was resected, and a large patent ductus arteriosus was divided. On the fourth postoperative day, he complained of abdominal pain. His blood pressure at this time was 150/125 mm Hg in both arms and legs. The white blood cell count ranged from 24 to 48 × 10^9/L. On the 14th postoperative day at laparotomy, there were punctate serosal hemorrhagic areas throughout the small bowel. In the ileum, there were three perforations and many scattered areas of spotty gangrene. Seventy centimeters of the ileum had to be removed. Microscopic sections of the mesenteric vessels and of the medium-sized and small arteries in the abdominal wall showed findings similar to those noted in the first patient. The patient recovered satisfactorily. Ten days after he was operated on, the blood pressure was 118/74 mm Hg in his arms and 124/84 mm Hg in his legs. Severe hypertension and arteritis suggested that overactivity of the sympathetic nervous system was the cause of these remarkable changes.

Soon after, the same abdominal complaint developed in a third patient, a 6-year-old girl, following removal of her coarctation. Preoperative blood pressures in her arms and legs were 190/40 mm Hg and 104/72 mm Hg, respectively. A moderate-sized ventricular septal defect was present. Forty-eight hours after the operation, the blood pressure

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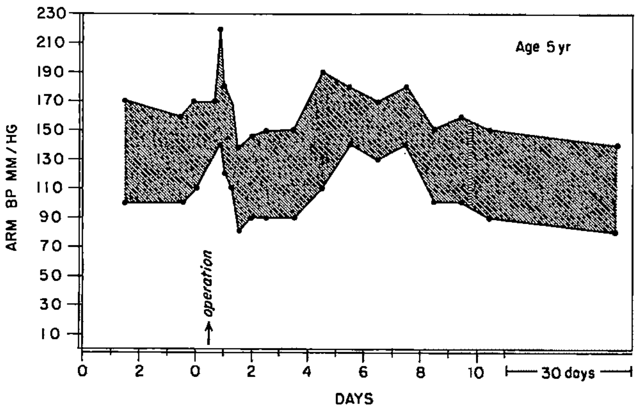

Fig 1. Blood pressure (BP) *record of a patient showing a marked elevation of the blood pressure immediately after operation. The second hypertensive response begins on the fourth day, and blood pressure approaches normal on the 30th day.*

in the arms was 190/140 mm Hg. At 72 hours, abdominal pain developed and she had a white blood cell count of 25 × 10^9 L [3]. On the assumption that overactivity of the sympathetic nervous system was present, intravenous hydralazine hydrochloride was given. The abdominal pain promptly disappeared, the white blood cell count decreased to normal, and the blood pressure decreased from 190/140 mm Hg to 150/70 mm Hg. Medication was continued for 10 days. She was discharged from the hospital with a blood pressure of 140/80 mm Hg in her arms and without symptoms. Very soon after this experience, 3 more patients were found to have the same signs and symptoms. In these patients, reserpine was used with equally good results.

The records of all patients with coarctation of the aorta on whom we had operated were then reviewed [1]. Postoperative hypertension was considered to be present when it was found to be higher than the preoperative level of the arm pressure. Although the blood pressure records in some patients were incomplete, 7 of 30 patients (23%) were found to have had marked elevation of blood pressure in the first 24 hours. In 1 patient, the systolic pressure was recorded as high as 230 mm Hg. One of the 7 patients progressed to the second response. Fourteen patients (47%) had a delayed hypertensive response 12 to 72 hours after operation.

When a prospectively observed group of patients was studied after removal of the coarctation [5], 26 of the 41 patients (63%) had the immediate hypertensive response. The second hypertensive response was found in 12 of the 41 patients (29%) but all 12 patients had the first response.

These two studies clearly separated the two postoperative hypertensive responses (Fig 1). The first response, occurring in more than one half of the patients, was not usually of more than 24-hours' duration. The second hypertensive response was frequently associated with abdominal pain.

The two postoperative hypertensive responses were not described in early reports of the surgical treatment of coarctation, but most detailed accounts since then have noted paradoxical hypertension [6–19]. One patient had the diagnosis made 3 months after repair [20]. Along with abdominal pain, paralysis developed in the lower half of his body secondary to arteritis of a spinal artery. Vasculitis including splenic and mesenteric artery rupture [4, 9, 21] and gastrointestinal bleeding have been reported [22]. Intestinal stricture developed in another patient 4 weeks after operation [10].

Although there are reports of arteritis in the mesenteric vessels [4, 8, 20–26], only two autopsy reports aside from the one outlined here describe the vascular lesions in areas other than the intestines [4, 20].

The cause of the first hypertensive response can be explained by the release of the stretch on the baroceptors in the carotid arteries and aortic arch after removal of the aortic obstruction. The best evidence for this is the marked increase in sympathetic activity indicated by elevations in norepinephrine level after operation greater than those found after other operations of similar magnitude [12, 26, 27]. The norepinephrine level remained elevated for up to 13 days in the Duke series (Fig 2) and for 6 months in the Benedict, Graham-Smith, and Fisher study [28]. The latter observers noted that only 2 of the 6 patients had the early hypertensive response, whereas 5 of the 6 patients had the second response. In the Duke series, 6 of 12 patients had elevated levels of norepinephrine with 5 of the 6 having the first and second responses.

Studies of baroreceptor sensitivity have been done only on postoperative coarctation patients who have chronic hypertension. As expected, they had a high set of the baroreceptors [29].

Baroreceptor activity in experimental coarctation investigated by Bonchek and Rees [30] showed only normal sensitivity. Experimental observations of Igler, Boerboom, and associates [31] indicated that the baroreceptor reset occurred after induction of coarctation, only to return to normal after coarctation repair.

The reason for the second hypertensive response is not clearly understood. The following facts are known. Pa-

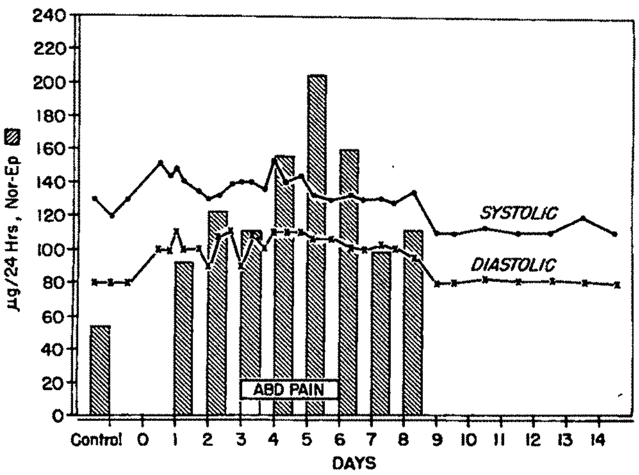

Fig 2. Great increase in excretion of norepinephrine (Nor-Ep) *in a 12-year-old patient after operation. This was associated with the two hypertensive responses and abdominal* (ABD) *pain.*

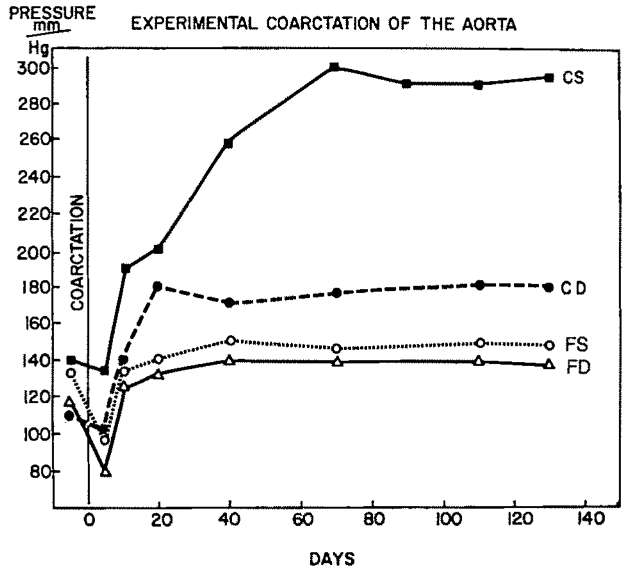

Fig 3. Coarctation of the aorta on the adult dog shows that the initial postcoarctation blood pressure is not elevated. Only at 14 days after operation do the pressures reach hypertensive level. Note that femoral pressures are stabilized slightly above the preoperative levels. (CS = carotid systolic; CD = carotid diastolic; FD = femoral diastolic; FS = femoral systolic.)

tients have increased sympathetic activity that continues well after the expected baroreceptor reset. The norepinephrine levels encountered indicate extreme levels of sympathetic activity, judged by the studies of Floras and associates [32]. In addition, the second hypertensive response can be reversed by reserpine, which causes a depletion of the adrenergic transmitter; by β-blocking agents [33]; by hydralazine hydrochloride, a smooth muscle relaxant; and by angiotensin converting enzyme inhibitors. Giddings and co-workers [34] showed that preoperatively administered propranolol prevented a hypertensive response in 7 patients, whereas hypertension developed in 4 of 7 patients of the control group.

That plasma renin activity would increase for 3 to 5 days after removal of the coarctation and that angiotensin II enzyme blocking agents will reverse the hypertensive responses is, to say the least, illogical [35–38]. The relationship between norepinephrine and angiotensin II, both potent vasoconstrictors, is complex [39–43]. None of these considerations explains exactly why blocking the action of one or the other hormone are equally effective in controlling paradoxical hypertension.

Experimental Coarctation of the Aorta

Coarctation of the aorta has been produced in adult dogs [44–48], puppies [30], and rats [49, 50]. The development of the hypertension resembles the pattern of the one-kidney, one-clip Goldblatt preparation [51] (Fig 3). Plasma renin activity increases immediately and remains elevated for 3 to 5 days [52–54]. The blood pressure above and below the coarctation site begins to increase in 3 to 5 days, at the time the plasma renin activity is returning to normal. The pressure continues to rise over the next 3 weeks or so, when one would expect collateral circulation to be increasing. The pressure below the coarctation reaches its precoarctation level in 14 to 21 days (Fig 3).

Added evidence that the kidneys play a role in hypertension of coarctation were the experiments of Scott and Bahnson [45, 46], who showed that moving a single remaining kidney above the experimental thoracic coarctation relieved the hypertension. Studies of renal dynamics in dogs with experimental coarctation have shown only an increase in the filtration fraction [55–57]. Svane and Jensen [58] reported microscopic evidence of juxtaglomerular hyperplasia.

Hypertension and Coarctation in Humans

The hypertension in coarctation of the aorta in humans has been the subject of both intense study and much speculation [59–65]. Sir Thomas Lewis [62] showed that the femoral pulse wave occurred later than the radial, opposite to the normal. He found normal blood flows in the legs. Direct arterial pressure measurements, notably those of Steele and Cohn [63], indicated that mean pressures below the coarctation were frequently at hypertensive levels and equal to the resting mean pressures above the coarctation. Wakim, Slaughter, and Clagett [64] found blood flows to be unchanged in the arms and legs before and after operation for coarctation. Patterson, Shepherd, and Whelan [65] found flows to be the same in the arms and legs, but the resistances in the arms were greater than those in the legs.

The cross-sectional area of the coarctation and collateral circulation vary tremendously from patient to patient. In an occasional neonate, congestive failure occurs, supposedly due to failure of collaterals to develop before birth [66–68]. Examples of heart failure corrected by repair of the coarctation in patients who have intracardiac lesions have also been reported [69]. In an attempt to supply blood flow demands to strictures below the coarctation, unusually high arterial pressures occur above the coarctation with exercise [70–72]. In one study [70], the systolic levels in 6 of 20 patients reached 300 to 360 mm Hg. Dahlback, Dahn, and Westling [71] found that in the femoral artery, mean pressures recorded during exercise did not change despite great increases above the coarctation, but cardiac output recorded during strenuous exercise increased from 5 to 10 L.

In a study of 20 patients with coarctation, Taylor and Donald [70] found 6 patients with clinically significant elevations of resting cardiac output. Nine of the 20 patients showed an increase in the pulmonary wedge pressure during exercise. Seven of 8 patients examined after operation were found to have a reversion of the pressure to normal levels. Three patients had an increase in the pulmonary artery pressure during exercise. The left ventricular work before operation was increased in all 20 patients over that of the normal control group. Do these observations indicate that the left ventricle may be stressed to its limits to supply blood flow to structures below the coarctation?

The great interest in 1930 to 1940 in the Goldblatt experiments [73, 74] led to several studies in humans trying to relate the hypertension in coarctation to the kidney [75–77]. Harris, Sealy, and DeMaria [77] reviewed the information then available on renal hemodynamics in coarctation and reported their observations on patients before and after operation. They concluded that there was no decrease in renal blood flow in coarctation and speculated that some other mechanism was a factor in causing the hypertension, in addition to the resistances at the coarctation site and in the collaterals.

When it became possible to determine more easily the plasma renin activity, this was measured in patients with coarctation [79–81]. Most showed no elevation in plasma renin activity before operation. Alpert and co-workers [80], in an excellent study on patients with coarctation, found that when furosemide was added to a low-sodium diet, marked elevations in plasma renin activity occurred. In addition, they found that plasma volume and extracellular fluid volume were increased, as was the cardiac output, and noted the similarity between coarctation and Goldblatt hypertension.

In a recent discussion of the hypertension in coarctation of the aorta, Schaffer [82] called attention to "the bipedal exercise triad." During exercise, an increase occurred in systolic pressure in the arms. The pressures in the legs were unchanged despite an increase in the systolic gradient across the coarctation. The response to exercise caused a shunting of blood to muscle from the kidney, which increased plasma renin activity.

Comment

The cardiovascular adaptations to a coarctation of the aorta are more complex than merely an elevated blood pressure above the coarctation and the development of collateral arterial channels around it. As the removal of the coarctation may cause two hypertensive responses, it is reasonable to assume that interruption of the need for the adaptations is related to these unexpected events. That such responses do not occur in every postoperative patient speaks of the wide variation among patients in the coarctation cross-sectional area and in the number and size of the collaterals. Thus in some patients, collateral development alone ensures blood flow to the structures below the coarctation.

The high set of the baroreceptors explains the first postoperative hypertensive response. The decrease in the stretch of the carotid and aortic baroreceptors by removal of the aortic obstruction causes greatly increased sympathetic activity that could be a factor in initiating a second response. The high set could be the result of the next adaptation noted below.

The adaptation that by increasing the pressure above the coarctation maintains normal renal blood flow has been compared with Goldblatt hypertension. There is one important difference between the two hypertensions. The kidneys have to share the blood flow getting through the coarctation. For example, the great flow demand that suddenly arises from strenuous muscle activity can increase the need from less than 800 mL/min to as much as 5,000 to 8,000 mL/min [83]. To meet this need during exercise in a tight stenosis, a great increase in the systolic blood pressure occurs above the coarctation to as much as 360 mm Hg. If the pressure increase above the coarctation fails to meet the flow needs of the exercising muscles below, are there other adaptations present that can ration the volume of blood that gets through the coarctation and through the collaterals to supply this demand? A part of this needed diversion to the muscle occurs directly to the muscles of the trunk and upper abdomen by the large collaterals, which may further reduce the blood volume available for the distal aorta.

Shunting of blood to structures of great need is a mechanism found in both physiological and pathological states. During exercise, there is a shift of blood to muscles to meet short-term needs. In heart failure and low-volume shock, blood may be shunted to the heart and brain from the kidney, the gastrointestinal tract, and the extremities. One of the most interesting examples of physiological shunting of blood to the site of greatest need is found among diving animals, in which blood flow to muscle, gut, and kidney is nearly all shunted to the heart–brain axis [84–86]. Weddell seals can actively search for food while submerged for as long as an hour. Folkow and co-workers [84] showed that in diving ducks, the arteries leading to the muscles but outside of them had high concentrations of adrenergic receptors. He believed that this mechanism permits the duck to reduce muscle blood flow by constriction of the large arteries despite the autoregulatory dilatation of the muscle's arteriolar bed.

One of the adaptations in coarctation during exercise could be a regional mechanism that would shunt blood to muscle from the kidney and gastrointestinal tract. Over the past several years, an array of substances have been found in the endothelium and the smooth muscle of the vessel walls that dilate and constrict the vessels and could play a role in this adaptation [87–91]. These include norepinephrine, angiotensin I and II, renin, and angiotensin converting enzyme. Prostaglandin and both relaxing and constricting endothelial substances are among the other paracrines and autocrines noted. These substances could be used for regulating regional flow by some mechanisms not yet understood.

As an indicator of activity of these substances, plasma renin activity in some patients is elevated for 3 to 5 days after correction of the coarctation, whereas norepinephrine levels are increased well above those found after other operations of the same magnitude. The hypertension continues after the angiotensin level returns to normal, although the angiotensin converting enzyme inhibitors are still effective in controlling the blood pressure and preventing the arteritis.

The dramatic morphological change in the arteries below the coarctation after operation may reflect another adaptation of these arteries to the coarctation. Theories explaining the pathogenesis of the arteritis in malignant and experimental hypertension fit the circumstances present after removal of the coarctation [92–101]. The sudden great increase in blood pressure in malignant hypertension is thought to cause the marked arteritis. In patients with coarctation, the arterial bed below the coarctation has been protected from high systolic pressures. This suddenly changes when the pressure is greatly elevated. The vessels below the coarctation perhaps respond as the entire arterial system does in malignant hypertension. This explanation leaves one with a degree of uncertainty. The increase in arterial muscle spasm is the principal cause of the hypertension. The spasm then becomes intense and persistent enough to cause ischemia of the arterial wall, followed by the severe changes. In coarctation, the destructive spasm only occurs below the coarctation in vessels conditioned or adapted to a greater capacity to respond.

The adaptation needed to make certain that distal exercise muscle flows are adequate could be activated by the removal of the coarctation in those patients with the second hypertensive response. If the theory is correct, the persistently elevated norepinephrine level and transiently elevated angiotensin II level may be indicators of this response. This mechanism can be shut down by substances that relax spasm of the arterial muscle and block the action of norepinephrine and angiotensin II. That this response is self-limited is shown by failure of the hypertension to recur after medication is stopped and the limited course that it runs in other patients not given specific medication.

Conclusion

Coarctation of the aorta can cause a series of complex cardiovascular responses, all adapted to maintaining the needed blood flow to organs below the stricture. Operation disrupts these adaptations and may cause two paradoxical hypertensive responses.

The presence of collaterals around the coarctation is the first adaptation. This may be all that is needed in many patients.

The second adaptation, similar to Goldblatt hypertension, causes an increase in the blood pressure above the coarctation to a level that maintains blood flow adequate for optimal kidney function.

The third adaptation is the high set of the carotid and aortic baroreceptors. An increase in blood pressure occurs for a few hours after operation until the baroreceptors are set at a lower level.

The fourth adaptation is a theoretical one. The arterial system contains a regional mechanism that during exercise shunts most or all of the blood reaching the distal aorta to the muscle. When the coarctation is removed, a signal is read indicating the start of exercise. After operation, the mechanism does not shut off and remains in effect until the arterial system below the resected coarctation virtually destroys itself.

Despite the still large gaps in our knowledge about these illogical hypertensive responses, an empirical approach to them years ago led to their near-absolute control. This has eliminated the chance for more detailed study of its most interesting aspect, the severe regional arteritis.

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CORRESPONDENCE

Repair of Thoracic Dissections

To the Editor:

In February 1989, we reported treating the ascending aorta with 25% glutaraldehyde solution before graft insertion in patients with type A thoracic aortic dissections [1]. Since the report, we have operated on 5 additional patients without technical difficulty in the same manner described in our report. However, we have recently encountered a serious complication that may have been related to glutaraldehyde usage. We wish to bring this problem to the readership's attention.

On January 28, 1990, a 65-year-old patient underwent resection of the ascending aorta from 5 mm above the coronary ostia to the mid transverse arch for an acute type A thoracic dissection. After the resection was completed, the proximal and distal ends of the remaining aorta were treated for 7 minutes with 25% glutaraldehyde-soaked cotton balls. The graft was sewn in place and the patient came off cardiopulmonary bypass without difficulty. However, the patient could not be weaned from positive-pressure ventilation and required tracheostomy on the 14th postoperative day. Three months later, we are still unable to wean the patient from the ventilator. We performed a phrenic nerve conduction study and found that when the phrenic nerves were stimulated percutaneously in the neck, neither diaphragm moved. In the laboratory, we found that when the phrenic nerve came in contact with 25% glutaraldehyde solution for 4.5 minutes, the nerve lost its ability to conduct. Conduction did not return 1 hour later when the experiment was terminated.

In the patient in question, we believe that the glutaraldehyde may have come in contact with the phrenic nerves as they pass around the aortic arch and caution that it is essential to protect the phrenic nerves with Silastic sheeting or some other form of impermeable barrier while applying the glutaraldehyde to the distal ascending aorta or aortic arch.

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Postoperative Drainage and Pericardial Effusion

To the Editor:

We read with interest the paper by Smulders and associates [1] showing that the incidence of postoperative pericardial effusion was not reduced by prolonging chest tube drainage time. We wish to draw attention to a similar recent study from our previous institution [2], where the criteria for drainage tube removal were standard but the placement of drainage tubes was not. Patients had either a single anterior mediastinal drainage tube or a posterior pericardial and an anterior mediastinal drainage tube. We found that posterior pericardial effusion was significantly more common in those with a single anterior chest tube, and in addition these patients had a significantly higher incidence of late postoperative tamponade. We therefore suggest that although duration of chest drainage may not alter the incidence of postoperative effusion, the positioning of drainage tubes may alter the incidence of both postoperative effusion and late cardiac tamponade.

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Reply

To the Editor:

In their paper, Angelini and co-workers convincingly demonstrated the risks of using only a single drainage tube placed in the anterior mediastinum. We agree that it is much safer to use both a posterior pericardial and an anterior mediastinal drainage tube. This conviction partly originates in our observation that, during the postoperative course, the pericardial and mediastinal drains often show completely different output patterns. This suggests that clots and/or newly formed fibrinous adhesions may soon separate the posterior pericardial and the anterior mediastinal space. This may happen even more readily if the pericardium is (partly) closed, which is recommendable because it facilitates possible reoperation and because the closed pericardium can act as a barrier against infection during the postoperative period. However, we feel that even if the pericardium is left open, a posterior pericardial chest tube is necessary to ensure the drainage of fluid accumulating behind the heart when the patient is in supine position during the early postoperative course, and thus to reduce the incidence of postoperative pericardial effusion and the risk of cardiac tamponade.

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Coronary Artery Bypass Grafting Without Splenectomy

To the Editor:

It was with considerable interest that I read the presentations of Thompson and associates [1] and Koike and colleagues [2] in consecutive issues of *The Annals*. Thompson and colleagues demonstrated the safety of performing cardiac operations in patients with idiopathic thrombocytopenic purpura (ITP) without prophylactic or concomitant splenectomy. On the other hand Koike and colleagues espoused simultaneous cardiac surgery and splenectomy "as an ideal surgical procedure" for ITP patients based on success with their patient.

As attested to by the cited references of these two papers the world's literature is not flooded with advice on how to handle the

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ITP patient in need of cardiac surgery. Having borne personal witness to the patient presented in Dr Thompson's paper, I drew from this experience in the following case.

A 53-year-old woman underwent cardiac catheterization for atypical chest pain and a borderline stress test. She had chronic ITP diagnosed 6 months previously. At the time of her cardiac catheterization she had been off steroids for 2 months and her platelet count was 65 × 10^9/L. During the procedure the left main coronary artery was dissected, extending down both the left anterior descending and circumflex coronary arteries with subsequent severe chest pain, S-T segment elevation, and cardiogenic shock. She underwent emergency coronary artery bypass grafting with reverse saphenous vein grafts to the left anterior descending coronary artery and an obtuse marginal branch of the circumflex. One gram of methylprednisolone was given intravenously before the induction of anesthesia. After cardiopulmonary bypass and the administration of protamine, 12 units of platelets and 0.3 μg/kg of arginine vasopressin were administered intravenously. An attempt to give γ-globulin as described by Schmidt [3] was aborted with less than half the calculated dose given because of induced hypotension. The first platelet count postoperatively was 130 × 10^9/L. There was no excessive bleeding. The platelet count remained greater than 100 × 10^9/L with continued steroid dosage, which was slowly tapered after 2 weeks.

This patient now represents the third reported ITP patient undergoing coronary artery bypass grafting without splenectomy. In view of this and the fact that not everyone with ITP requires splenectomy it is difficult to categorize concomitant CABG and splenectomy as "ideal." These patients certainly pose the risk of hemorrhagic complications, but I believe their treatment has to be individualized. Preoperative in vivo assessment of platelet dynamics as performed by Thompson and associates is certainly worthwhile as is assessment of steroid response. Splenectomy should be reserved for those who demonstrate a bleeding problem after platelet transfusion and steroids, and thrombocytopenia is the culprit.

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Reply
To the Editor:

Doctor Thompson and associates [1] indicate that use of cardiopulmonary bypass in patients with ITP does not invariably mandate splenectomy. It is a fact that corticosteroid or massive γ-globulin administration offer clinical remissions, and not everyone with ITP requires splenectomy. Splenectomy should be indicated in some patients with chronic ITP in whom such a medical therapy is not effective.

In our patient [2], aggravation of angina pectoris was induced by preoperative γ-globulin administration, but the increase in platelets was not enough. He also experienced ventricular arrhythmia during coronary angiography due to contrast media injection. His coronary artery was considered to be very sensitive to increased blood viscosity caused by massive γ-globulin, contrast media, or the increase in platelets. The patient's status was chronic and did not respond to medical therapy. Splenectomy as well as coronary revascularization was considered to be necessary for him.

We thought that a one-stage operation was convenient for the patient because he could resume his normal life and return to work after a few months, instead of returning to the hospital for a second operation, splenectomy.

Considering his younger age, we performed the one-stage operation of coronary revascularization using arterial grafting and splenectomy, although there was no previous report. We have preferentially been performing a gastroepiploic artery–right coronary artery anastomosis instead of using the right internal mammary artery. The dissection and division of the gastroepiploic artery, however, does not compromise the organs in the abdomen from our clinical experience. Splenectomy itself is not a serious invasion as coronary revascularization using the splenic artery has been reported [3].

Of great importance is the choice of conduit in such a patient: vein graft or arterial graft? Victorzon and co-workers [4] reported that not only native coronary artery but also saphenous vein revealed hyperconstriction in response to endogenous serotonin released from circulating platelets. Homcy and associates [5] reported that long-term administration of steroids made saphenous vein fragile. In the patients on steroids with platelet disorders, saphenous vein may be highly occluded. So, arterial graft should be the graft of choice.

We emphasize that GEA grafting is very convenient for revascularization in the patients requiring laparotomy as described above.

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Closed Chest Cardiac Massage
To the Editor:

I read with interest Classics in Thoracic Surgery, "The Introduction of Closed Chest Cardiac Massage," by Steven F. Bolling [1]. When I read it my memory flew back to around 1958 when Dr Hugh A. Stout stopped me in the hallway of Mercy Hospital in

Oklahoma City to tell me about what he thought would be a very important contribution to the general field of medicine. He described to me cardiac massage without incision and referred me to his paper [2]. I was introduced by Dr Hugh Stout to closed cardiac massage before it was systematized by Dr William Kouwenhoven. I will quote a few passages from the article by Dr Stout [2].

> What I hope to propose here is something more physiologically sound, more effective and something that should produce better long-term good results than kneading hearts.
>
> . . . and that the entire problem can be approached more sanely and more scientifically . . .
>
> . . . encounter with cardiac arrest in my own office. We were in the process of doing a sternal bone marrow aspiration on a young adult who had been previously in good health except for a moderate anemia for some months, with hemoglobin levels ranging from 7.5 to 10 grams and poor response to usual therapy . . .
>
> The above mentioned patient suddenly seemed to die while the pain was at its worst because the head fell to one side, the heart stopped beating, and respirations were not coming back while we tried elevation of the feet and artificial respiration compressing the thoracic cage. The patient was lying on his back and it occurred to me from an experiment which I had seen Doctor Krogh demonstrate in 1938, that something much better might be done. Doctor Krogh showed that almost a gallon of blood will gravitate into the legs when the feet are inclined downward while the patient is lying on a table on his back, as demonstrated by later inclining the head downward and the feet up.
>
> I therefore put my right arm under the patient's knees and jack-knifed the patient, thrusting the knees up into the epigastrium and on to the lower chest, actually rocking the hips up off the table with buttocks higher than the heart.
>
> By using a knee-pumping action, then, pressing the knees together and pressing the thigh muscles against the abdomen and lower chest, then relaxing the knees to vertical, and the back to horizontal position, one can continue this knee-pumping action at sixty or more times per minute and not only dilate the heart from the inside with a bellows-type action, but throw columns of pressure also up the aorta into the arch where the cardiac nerve plexuses are located with afferent sympathetic stimuli being made available to the vasomotor center of the brain,
>
> . . . but so far, I have not been able to find in the literature any description of this particular technique for revival after cardiac arrest. The usual procedure is to stick needles into the patient's heart, or nowadays to make a sudden incision over the heart, thrust the hand between the ribs and massage the heart, and rarely when available use an electrical stimulator.
>
> One man recently has tried hammering on the chest with success, although personally this does not seem to me to be the most logical method of revival.
>
> The brain can do without its blood supply for at least four minutes and return to normal so that there is plenty of time to use a method other than surgical massage.
>
> At least some standardized exercise should be recommended and automatically tried in a sufficient number of cases to become a standard procedure, preceding manual massage, and I would like to recommend the method proposed here, at least as a preliminary measure until some more scientific and constantly reliable method is established.

So, it is my feeling that the introduction of closed cardiac massage should be attributed to Dr Hugh A. Stout, fully acknowledging Dr Kouwenhoven's later contribution.

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To the Editor:

I read with great interest the historical review by Bolling [1] regarding the pioneering work of Kouwenhoven on closed chest cardiac massage. Although Kouwenhoven's work is certainly a milestone and the first evaluation of the method, to keep an appropriate historical perspective one is obliged to mention the case published in the October 24, 1858, issue of the *Orvosi Hetilap* from the pen of Janos Balassa [2], at the time Professor of Surgery at the University of Pest, Hungary.

In his paper, Balassa reports that on October 4, 1858, he was urgently summoned to the bed of an 18-year-old woman suffering from ulcerated laryngitis. While making preparations for a tracheotomy, Balassa witnessed the clinical death of the patient:

> . . . she lifelessly collapsed, her tense shoulders and arms became flaccid, her cyanotic face became a mask of death, her chest did not move any more and the pulsation of the arteries and heart ceased. The fearful thrust of the last and painful breath transformed her from living into death and made seemingly any further try and endeavor hopeless; but still her demise was so recent that it would have been a dare not to do everything possible to restore the breath ceased and to try to recall the life just passed! Therefore, I hastily pierced the ligament between the thyroid and the conoid cartilage—ligam conoideum—and inserted a Thompson tracheostomy instrument . . . At the same time, I exerted bellows-like rhythmic pressure to the front of her chest imitating breathing. While air entered the lungs with a sharp whistling sound, I splashed quickly fresh water into the face of my patient and held a vinegar dipped cloth in front of the opening on the tracheostomy tube. Close to six minutes passed without her moving at all and without the slightest signs of life. With my hopes lost I was close to suspending further attempts when she rejoiced me with a hasty and spontaneous sigh-like inspiration which was supported by the movement of my hand. This was followed by a second and third breath, and from the struggle of death life began to smile at us. After that her breathing became regular, heartbeat and pulses returned, the dark blue color of the face faded gradually, and her death-like expression changed into joyful appearance of life; and when, after 15 minutes, through which she remained unconscious, I called the patient loud by name,

> she lifted her heavy eyelids and signalled the return of her consciousness with a feeble smile [2].

I believe that the words of Balassa conclusively prove that he indeed resuscitated his patient with external heart massage.

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Pediatric Heart Transplantation

To the Editor:

We note with interest the experience of pediatric heart transplantation reported by Trento and associates in a recent edition of *The Annals* [1]. We have concerns, however, about their postoperative mortality and incidence of late complications. At our institute we have performed 10 heart transplantations on children aged 6 to 17 years (mean age, 13 years). Eight survive at 0.7 to 5.3 years after operation (mean, 3.5 years). Actuarial survival at 1 and 4 years was 80%. Two deaths occurred at 9 and 64 days from acute rejection and a cerebrovascular event, respectively. All 8 survivors enjoy an unrestricted life style and none have evidence of serious coronary occlusive disease on follow-up coronary angiography. One patient experienced an Epstein-Barr virus-related lymphoma, which was successfully treated with acyclovir and reduction in immunosuppression. Maintenance immunosuppression was with cyclosporine and azathioprine. Steroids were used continuously in the first 3 postoperative months and thereafter only for the treatment of rejection episodes. The dose of cyclosporine was adjusted to maintain whole blood cyclosporine levels between 200 and 500 μg/L (specific monoclonal assay). This was associated with mild elevation of the serum creatinine level in all patients (mean creatinine levels at 2 and 4 years after transplant were 1.44 mg/100 mL and 1.63 mg/100 mL, respectively).

Although our series is smaller, these data differ considerably from those of Trento and associates, who reported an actuarial survival at 6 years of 36%. Also, 50% of their patients were found to have graft-related atherosclerosis at 3 years. We noted that all patients in the Pittsburgh series required continuous steroid therapy because of recurrent rejection, but the cyclosporine dose was reduced substantially after 6 months. We suggest that at least in part these differences can be attributed to our improved management of immunosuppressive therapy. We accept some degree of renal impairment as an inevitable consequence of improved graft and patient survival, which is of particular importance when extending this form of therapy to children.

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Reply

To the Editor:

Obviously I am quite pleased and impressed with the results that Smyth and colleagues are reporting. I think that one of the major differences between our experience and that of Papworth Hospital is that we presented a series of heart transplantations in pediatric patients dating from 1982, and at least some of the deaths reflect a learning curve in immunosuppressive therapy regimens early in our experience. Regarding the incidence of coronary artery disease in their patient population, I suppose that they documented the absence of coronary disease with yearly coronary angiography in each of their patients, as we did. We define coronary artery disease as any degree of angiographically detectable coronary lesion. I do not think that we can derive any conclusion on the etiology of this complication from their experience as compared with ours. Finally, I am pleased to see that other groups have very good results and survival rates with pediatric patients, as has also been our experience more recently.

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Internal Mammary Artery Marker

To the Editor:

For a number of years, surgeons have used the internal mammary artery (IMA) as the conduit of choice for bypass of the left anterior descending coronary artery, and frequently as a sequential graft including the diagonal coronary artery. As time passes, more and more patients are being seen for reoperation with all of their saphenous vein grafts closed and the viability of their myocardium dependent on a patent IMA graft. Reoperation is particularly hazardous in this group of patients, as unintentional division of the IMA in this setting can be rapidly fatal.

I wish to report a technique that I have used for several years to aid in this situation. After completing the anastomosis of the IMA to the left anterior descending coronary artery, we take the radiopaque marker from a 4 × 4-inch gauze sponge and secure it with small clips to the right lateral edge of the IMA pedicle. This serves a dual purpose: first, the radiopaque marker allows a subsequent surgeon to analyze the position of the IMA pedicle on the posteroanterior and lateral chest roentgenogram and anticipate its relation to a subsequent repeat sternotomy incision, and second, the surgeon will encounter the blue marker in the scar tissue before being able to divide the IMA during the dissection. I have had the opportunity to reoperate on 2 patients in whom I had previously marked the IMA with this technique. I found it to be a substantial aid in avoiding damage to the patent IMA graft.

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Vein Graft Permeability
To the Editor:

The interesting article by Finck and co-workers [1] in the November 1989 issue of *The Annals* describes measurement of whole-tissue radioactivity (counts/g/5 min) of autologous internal jugular vein used as a carotid artery bypass graft in 9 dogs, compared with the ipsilateral internal jugular vein in animals killed 24 hours after injection of label at 1, 2, and 3 months. Further evidence of changes in the arterialized vein are provided by scanning electron microscopy (Fig 2B shows what seem to be three activated platelets, not mentioned in the caption or text) and by staining with Evans blue dye. Not mentioned in the Materials and Methods section is whether tissue counts were corrected for labeled plasma in the specimens by serial sampling of the blood after injection of label. Finck and co-workers have commented on the wide range of values within each group, and the inability to conclude whether radioiodinated albumin uptake was truly increasing with time. Using the published values for plasma volume in the dog [2], the range of plasma volume in the animals in this study would be 950 to 1,500 mL, an unknown fraction of which was in the tissue vascular space, which may explain the wide range of values. It would be helpful to know whether tissue radioactivity was corrected by estimates of unbound ^{125}I, and how the time interval of 24 hours for equilibration of exchangeable albumin pools was selected; in humans, this has been reported to be 4 to 5 days [3].

We have had a similar interest, and have found increased ^{125}I-labeled albumin flux into human saphenous veins distended at operation in comparison with the same vein before distention [4, 5], and will follow the future work of Finck and co-workers with interest. There is a typographical error in Table 1; the mean difference between graft and control in animals 7 through 9 should be 3.67, not 3.77.

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2. Altman PL, Dittmer DS, eds. Biological handbooks, respiration and circulation, 147, Blood volumes. Washington, DC: American Physiological Society, 1974:391.
3. Rothschild MA, Bauman A, Yalow RS, Berson SA. Tissue distribution of I^{131} labeled human serum albumin following intravenous administration. J Clin Invest 1955;34:1354–8.
4. Kennedy JH, Tedgui A, Juan L, Lavergne A, Piwnica A. Effect of preoperative hypertension on ^{125}I albumin uptake by vein graft media. J Cardiovasc Surg 1989;30:985–8.
5. Kennedy JH, Lever MJ, Addis BJ, Paneth M. Changes in vein interstitium following distension for aortocoronary bypass. J Cardiovasc Surg 1989;30:992–5.

Reply
To the Editor:

We thank Drs Kennedy, Tedgui, and Piwnica for their interest in our recent article. Tissue counts were not corrected for labeled plasma in the specimens. Serial sampling of the blood after the injection of the label would have allowed calculation of the influx rate of albumin into the vein wall (tissue radioactivity divided by specific activity of serum albumin) [1]. Expressing the results in this manner might have narrowed the range of results within each group of dogs. However, because of the small number of dogs in each group, we doubt whether any conclusions could have been drawn about increases in endothelial permeability with time.

We chose to harvest our vein grafts 24 hours after administration of Evans blue dye and ^{125}I-labeled albumin. This was done, in part, because of our previous experience and work by others with Evans blue dye uptake by arterial endothelium [1, 2]. We also chose the 24-hour interval because of reported stable serum iodinated albumin activity at this time [2].

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Jay P. Mashburn, MD
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References

1. Bell FP, Adamson IL, Schwartz CJ. Aortic endothelial permeability to albumin: focal and regional patterns of uptake and transmural distribution of ^{131}I-albumin in the young pig. Exp Mol Pathol 1974;20:57–68.
2. Finck S, Walker J, Vaccaro PS, Kakos GS, Howanitz EP, Cornhill JF. The effect of ischemia on canine carotid endothelial permeability. J Surg Res 1986;41:419–24.

Is Systemic Cooling Essential for Open Heart Surgery?
To the Editor:

Doctor Bigelow had a dream: "cool the whole body, reduce oxygen requirements, and interrupt the circulation and open the heart" [1]. His dream led to open heart surgery. Today, however, with refined anesthesiology techniques and pump oxygenator systems, cooling the whole body appears superfluous. It would suffice to cool the heart for myocardial protection by infusion of cold cardioplegic solutions. We do not use the cooler of the heat exchange unit. Only the heater is used to correct the spontaneous temperature drift. The technique has contributed to decrease pump time, need for vasodilators, postoperative ventilation, and incidence of arrhythmias. Is core cooling necessary today? It appears to be necessary only when there is a need to protect the brain as in operations on the aortic arch.

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Reference

1. Sealy WC. Hypothermia: its possible role in cardiac surgery. Ann Thorac Surg 1989;47:788–91.

Organ Procurement for Pulmonary Transplantation

To the Editor:

We read with great interest the excellent article on organ procurement for pulmonary transplantation written by M. Zenati and collaborators [1]. On our side, before starting lung transplantation, we studied the problems of lung donor selection and maintenance when harvesting heart, liver, and kidneys from brain-dead donors [2]. In one year (1986) we reviewed the lungs of 25 donors: 14 had died after a traffic injury (mean age, 23.8 years), 6 from a brain wound (mean age, 32 years), and 5 from a spontaneous cerebral hemorrhage (mean age, 37 years).

Lung biopsies were performed after other organs were harvested, the ventilation having been stopped for between 45 and 90 minutes (mean time, 70 minutes). All lungs had small areas of atelectasis and edema, especially in the dorsal and basal parts. Upper and lower lobes were biopsied.

Nineteen donors, whose mean age was 29 years, had a macrophagic alveolitis with presence of dust due to tobacco-smoking and environment; 6 donors had none of these aspects, and their mean age was 21.7 years. Nineteen had emphysematous lesions considered consequences of ventilation; the ventilation time was 16.4 hours versus 13.7 hours for the patients without such lesions. Atelectasis was observed in 6 donors, with no correlation with age, cause of death, or duration of ventilation. Three donors had a bronchopulmonary infection (in 1 case gastric fluid had been inhaled). Mean time of ventilation was not greater in these cases: 15.6 hours versus 15.2 hours. There was no correlation between the cases of infection and results of a systematic tracheobronchial bacteriological study.

In 17 donors interstitial vascular alterations produced by shock and subsequent edema were detailed: interstitial or alveolar fluid accumulation (15), lymphatic stasis (10), intracapillary infiltration of polymorphonuclear lymphocytes or monocytes (13), and thrombosis (9). Six lungs out of 17 had the four types of lesions. Mean duration of ventilation was 16.3 hours for these 17 donors versus 12.9 hours for the 8 donors who had no such lesions. No donor with a brain wound had such lesions. These 17 donors had been more perfused (170 mL/h difference), and the most severe lesions corresponded with the highest blood products/crystalloids ratio (0.582 versus 0.184, $p < 0.01$).

When selecting a donor for lung transplantation, one must answer two questions: are there pulmonary lesions preventing transplantation, and are there criteria to predict them? Lesions that are produced by tobacco smoking or environment are similar to those found in a population comparable for age and habits.

In 90% of cases potential donor lungs have lesions that are in relation with the cause of death and conditions of intensive care. Bronchial inertia and decrease of alveolar macrophage properties is observed in 25% of cases. Bacterial infection of the trachea is constant; bronchioalveolar infection is less frequent (12% in our series). The rate of traumatic emphysema (80%) can be decreased by better technique of ventilation. Edema is due to the surfactant's degeneration and changes in microcirculation. Maintenance of hemodynamics and diuresis can aggravate these lesions. Serum albumin and plasma can contribute to them, increasing alveolar capillary permeability. As far as the lung is concerned, management of donors should include antidiuretic hormones in cases of excessive diuresis (200 mL/h) to avoid excessive intravenous fluid intake, and vasopressive amines at moderate doses as well as concentrated blood and crystalloids in cases of hemorrhage to keep sufficient pulmonary arterial pressure without edema. Should edema appear, fluid administration must be reduced and diuretics must be used. In conclusion, apart from unavoidable conditions, lung procurement should aim at a shorter duration of ventilation when possible, and at a hemodynamic management based more on cardiac status and blood pressure than on vascular repletion and diuresis.

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References

1. Zenati M, Dowling RD, Armitage JN, et al. Organ procurement for pulmonary transplantation. Ann Thorac Surg 1989;48:882–6.
2. Pruvot FR, Sault MC, Duquennoy O, et al. Le poumon des sujets en état de mort cérébrale. Corrélations anatomo-biologiques en vue de la transplantation pulmonaire. La Presse Med 1989;18:480–3.

Reply

To the Editor:

Doctors Ribet and Pruvot offer some interesting observations regarding the microscopic appearance of lungs accepted for pulmonary donation. Ventilator injury and fluid overload were thought to be the causative factors. They do not, however, provide any evidence that their findings could be correlated with measurable changes in outcome after transplantation. Ventilation times quoted ranged from 12 to 16 hours, which is considerably less than the 1- to 2-day average ventilation times for our donor population.

Ventilator-induced injury has not been a factor in our program. Although prolonged ventilation should be avoided, we would disagree that short periods of ventilation are necessarily desirable. We have found serial determinations of oxygenation to be very useful in identifying potential donors who appear to be acceptable early on but then manifest previously occult damage as evidenced by a deterioration in arterial oxygenation.

Most donors today must be managed for multiple organ donation with conflicting requirements for fluid and pharmacological support. With regard to the lungs, we accept systemic systolic blood pressures of 100 mm Hg and attempt to maintain this level with judicious use of both crystalloids and vasopressors. Diabetes insipidus is usually managed with vasopressin.

As our experience with organ procurement has grown, we have modified donor selection criteria to reflect variables identified to have significant impact on recipient survival. Our most recent change involves antibiotic prophylaxis to the donor and recipient following our discovery of the importance of donor mouth flora in the development of early thoracic infection after transplantation [1]. To further modify ventilator and fluid management of potential donors without sufficient proof is not practical given the varied nature and location of the hospitals providing donors for our pulmonary transplant program.

Bartley P. Griffith

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Reference

1. Zenati M, Dowling RD, Dummer JS, et al. Influence of the donor lung on the development of early infections in lung transplant recipients. J Heart Transplant (in press).

Hypoxemia During Cardiopulmonary Bypass

To the Editor:

We agree that hard data on oxygenator problems and accidents are scarce and a database should be set up. However, the following points should be noted regarding the report by Robblee and associates [1]. In general, if gas flow becomes interrupted, diverted, or reduced below a minimum then whatever fluid is present immediately above the gas disparger plate will enter the gas compartment by gravity. Once there, any liquid or solid phase material will affect predictability and stability of gas exchange. Manufacturers recommend continuous running of gas at approximately 1 to 1.5 L/min to prevent this occurring. If ingress occurs before bypass, clear liquids may be blown through with high gas flows; if this is not 100% effective the oxygenator must be changed. We consider the likely cause of the problem to have been interruption of the gas flow after the first bypass. It is a useful safety measure to maintain gas flow until the circuit is dismantled.

When the manufacturers' recommendations have been flouted, it is meaningless to blame the mannitol even if conditions are recreated experimentally.

We encountered a somewhat different problem during a routine coronary artery operation. Shortly after completion of the first distal anastomosis an audible hissing developed. Arterial oxygen tension was then 29.4 kPa. Connections were checked but the hiss continued and arterial return blood darkened visibly. Within 8 minutes the oxygenator (William Harvey H 1700) had stopped bubbling. The patient by this point had been reventilated and bypass was stopped easily at 35°C with a systolic blood pressure of 95 to 100 mm Hg and no inotropes. The oxygenator was changed, the operation completed, and the patient extubated at the end of the procedure. There was no neurological deficit. Careful inspection revealed a circumferential crack in the Luer fitting on the gas line that had allowed blood to enter the gas compartment.

We consider it fortunate that the operation was being carried out at near normothermia using an intermittent fibrillation technique; this allowed quick recovery and easy cessation of bypass.

We emphasize that interruption of the gas supply from whatever cause will allow liquid into the gas compartment and may cause rapid failure of bubble oxygenators.

Philip Belcher, MB, BS, FRCS
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Reference

1. Robblee JA, Crosby E, Keon WJ. Hypoxemia after intraluminal oxygen line obstruction during cardiopulmonary bypass. Ann Thorac Surg 1989;48:575–6.

Inadequate Flow of the Internal Mammary Artery: Another Complication of Sternal Overretraction

To the Editor:

The internal mammary artery is universally accepted as the conduit of choice for patients undergoing coronary artery bypass grafting. The use of the left internal mammary artery (LIMA) is recommended in almost all patients. The LIMA is harvested in the standard fashion by completely mobilizing the pedicle up to the subclavian vein and dividing all the branches. Flow is usually checked immediately after mobilization to decide if the LIMA is to be used as a pedicle or as a free graft.

We recently encountered a patient who had excellent flow of his LIMA after mobilization. The mammary artery was prepared and put in a papaverine sponge to be used later. After two distal vein graft anastomoses, the LIMA to left anterior descending coronary artery anastomosis was performed. Just before the completion of the anastomosis the bulldog clamp was released and no mammary artery flow was observed. The vessel was gently probed past the clamp site without evidence of spasm, obstruction, or dissection and without obtaining any blood flow. We therefore decided to use the LIMA as a free graft. The artery was cut proximally and saline solution was instilled in the antegrade fashion without a problem. Of note is that the proximal cut end of the LIMA still did not bleed. After completion of the aortic anastomosis the cross-clamp was released. Normal sinus rythm was restored spontaneously and the patient was weaned from cardiopulmonary bypass. On closing the retractor massive bleeding was noted from the proximal cut end of the LIMA, which was then ligated. We concluded that the interruption of blood flow from the LIMA was caused by overretraction of the sternum. This must have caused stretching and kinking of the LIMA at its origin from the subclavian artery. In retrospect the retractor was opened further at the time of the distal anastomosis and after flow through the LIMA was already checked.

Reported complications of overretraction of the sternum include avulsion of the innominate vein, stretching of the brachial plexus. and increased pulmonary inflation pressures. The purpose of this letter is to increase awareness of another possible complication of sternal overretraction, ie, interruption of LIMA flow. It seems logical that excessive retraction of the sternum may also decrease the flow in the LIMA. Consequently when LIMA flow is measured, we recommend slightly closing the retractor before deciding that LIMA flow is unsatisfactory.

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Sternotomy Infections in Infants

To the Editor:

We read with interest the recent report of treatment of median sternotomy infection and sternal necrosis in an infant by Drs Terranova and Crawford of the Medical University of South Carolina [1].

In 1988 we published a series of 8 infants with sternotomy wounds, 5 of whom underwent muscle flap reconstruction [2]. Their ages ranged from 1 to 10 months with each weighing between 3 and 7 kg. This series had been presented at the European Cardiothoracic Society Meeting in Vienna, Austria, in 1987; The World Congress of Pediatric Cardiac Surgery in Bergamo, Italy, in 1988; and the American Society of Plastic and Reconstructive Surgeons in Atlanta, Georgia, in 1987.

All patients underwent bilateral pectoralis major advancement flaps with 3 of the 5 patients requiring simultaneous use of a rectus abdominis muscle flap. We, too, have noted the diminutive nature of the muscle flaps and vascular pedicles that require loupe magnification for their elevation and bipolar electrocautery for safe but "assiduous" hemostasis. We have found, however, that the use of a cutaneous territory to form a musculocutaneous flap or the use of a split-thickness skin graft applied to the uncovered muscle as advocated by Drs Terranova and Crawford is not only unnecessary and more involved but aesthetically unpleasing. Mobilization of adjacent pectoral cutaneous flaps virtually always suffices for the completion of the closure overlying the transposed muscular units.

In reconstructing sternotomy wounds in female patients, however, wide mobilization of such pectoral flaps is relatively contraindicated to prevent damage to undeveloped breast buds. Therefore, in cases in which rectus abdominis flap(s) will suffice for the obturation of such wounds in female patients, a skin graft or skin island would help preserve otherwise undisturbed presumptive breast tissue.

We are encouraged by the appearance of this case report and other publications that have appeared subsequent to our publication [3], as we feel that this modality of treatment is safe and efficacious in this age group.

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References

1. Terranova W, Crawford FA Jr. Treatment of median sternotomy wound infection and sternal necrosis in an infant. Ann Thorac Surg 1989;48:122–3.
2. Stahl RS, Kopf GS. Reconstruction of infant thoracic wounds. Plast Reconstr Surg 1988;82:1000.
3. Gault DT, Huddleston C, Jones BM. Infected sternotomy wounds. Eur J Cardiothorac Surg 1990;4:48–50.

Reply

To the Editor:

We acknowledge the report of Stahl and associates published in December of 1988 in *Plastic and Reconstructive Surgery*. Our case report was submitted for publication before this date, and we were unaware of it at the time. Our report additionally stressed the ease of a second operative procedure through the same median approach, a point not made in their article.

We would agree that direct skin closure over the muscle flaps is to be preferred. In this situation, however, direct closure could be obtained only at the risk of flap viability. Therefore, a skin graft, although "aesthetically unpleasing," was necessary.

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CORRECTION

In the article entitled "Prostaglandin E_1 and intrapulmonary shunt in cardiac surgical patients with pulmonary hypertension," by Paul M. Heerdt, MD, PhD, and Carey I. Weiss, MD, published in the March 1990 issue of *The Annals of Thoracic Surgery* (1990;49:463–5), the formulas contained a printing error. The corrected formulas are as follows:

$$\mathrm{CcO_2} = \text{oxygen content of pulmonary capillary blood}$$
$$(\mathrm{Hb} \times 1.39)\mathrm{SAO_2} + (\mathrm{PAO_2} \times 0.0031)$$

$$\mathrm{CaO_2} = \text{oxygen content of arterial blood}$$
$$(\mathrm{Hb} \times 1.39)\mathrm{SaO_2} + (\mathrm{PaO_2} \times 0.0031)$$

$$\mathrm{CvO_2} = \text{oxygen content of venous blood}$$
$$(\mathrm{Hb} \times 1.39)\mathrm{SvO_2} + (\mathrm{PvO_2} \times 0.0031)$$

$\mathrm{PaO_2}$ = arterial oxygen tension; $\mathrm{PAO_2}$ = oxygen tension of pulmonary capillary blood (from alveolar gas equation); $\mathrm{PvO_2}$ = venous oxygen tension; $\mathrm{SaO_2}$ = oxygen saturation of arterial blood; $\mathrm{SAO_2}$ = oxygen saturation of pulmonary capillary blood; and $\mathrm{SvO_2}$ = oxygen saturation of venous blood.

The Annals regrets the error.

PROGRAM

1990 INTERIM MEETING THE SOCIETY OF THORACIC SURGEONS

September 21–23, 1990
Hyatt Regency Chicago, Chicago, Illinois

Friday, September 21, 1990

1:00 **Opening Remarks**
Welcome
W. Gerald Rainer, President

Introduction to Program
Richard P. Anderson, Secretary and Interim Meeting Program Chairman

1:10–2:45 **Medico-Legal Session**
Moderator: Thomas D. Bartley, Chairman, Committee on Medico-Legal Affairs

STS Professional Liability Survey
Thomas D. Bartley

The AMA/Specialty Society Medical Liability Project
James S. Todd
Executive Vice President, American Medical Association

California Tort Reform
Winfield J. Wells
Member, Committee on Medico-Legal Affairs

A Trial Lawyer's Perspective
Joseph D. Jamail
From the firm of Jamail and Kolius, Houston, TX

INTERMISSION

3:30–5:00 **Health Care in America**
Moderator: Richard P. Anderson

Health Care Needs—The Consumer Viewpoint
Robert E. McGarrah, Jr
Director for Public Policy, American Federation of State, County, and Municipal Employees

Health Care—A Political Perspective
The Honorable Richard D. Lamm
Professor, Leo Block Chair, Director, Center for Public Policy and Contemporary Issues, The University of Denver; Governor of Colorado, 1975–1987

The Health Care Industry
Austin Ross
Vice President and Executive Administrator, Virginia Mason Medical Center; Chairman, Ad Hoc Committee on Physician Involvement, American Hospital Association

Saturday, September 22, 1990

7:00–11:00 **Workshops on Reimbursement and Coding** (By separate registration)

7:00–8:30 **Physicians' Session**
This session will feature a representative from HCFA discussing recent changes affecting cardiothoracic reimbursement.

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9:00–11:00 **Coding Workshop for Office Personnel** (Physicians welcome)
Experts on CPT-4 and ICD-9 will explain the two coding systems and answer questions related to cardiothoracic billing.

MORNING PLENARY SESSION

8:30–9:45 **Physician Reimbursement**
Moderator: W. Gerald Rainer

The Canadian Experience
Hugh E. Scully
Member, Committee on Physician Reimbursement

Thoracic Surgery Initiatives
George E. Miller, Jr
Chairman, Committee on Physician Reimbursement

INTERMISSION

10:30–12:00 **Physician Reimbursement, continued**

Paul B. Ginsburg
Executive Director, Physician Payment Review Commission
Washington, DC

Monica Noether
Senior Economist, Abt Associates, Inc
Cambridge, Massachusetts

Glenn R. Markus
STS Consultant on Physician Reimbursement and Government Relations
Health Policy Alternatives, Inc
Washington, DC

12:00–1:30 Luncheon
The Honorable Louis W. Sullivan
Secretary, Department of Health and Human Services

AFTERNOON SCIENTIFIC PROGRAM

2:00–5:45 **THREE PARALLEL SCIENTIFIC SESSIONS**

Session I: General Thoracic Surgery

2:00 Management of Stage IIIA Lung Cancer
Robert J. Ginsberg, New York, NY

2:20 Management of Barrett's Esophagus
F. Henry Ellis, Jr, Burlington, MA

2:40 Esophageal Diverticula
Mark B. Orringer, Ann Arbor, MI

3:00 Pulmonary Resection for Metastatic Disease
Thomas R. J. Todd, Toronto, Ont, Canada

INTERMISSION

4:10 Multimodality Treatment of Cancer of the Esophagus
Joseph I. Miller, Atlanta, GA

4:30 Mesothelioma
Nael Martini, New York, NY

Parallel Scientific Sessions, continued

4:50 Pancoast Tumor
Harold C. Urschel, Jr, Dallas, TX

5:10 Management of Achalasia
Mark K. Ferguson, Chicago, IL

Session II: Adult Cardiac Surgery

2:00 Challenges for Cardiac Transplantation in the Nineties
Bartley P. Griffith, Pittsburgh, PA

2:20 Heart-Lung Transplantation—1990
Bruce A. Reitz, Baltimore, MD

2:40 Current Status of Mechanical Circulatory Support
D. Glenn Pennington, St. Louis, MO

3:00 Cardiac Arrhythmia Surgery: Current Status and Future Directions
James L. Cox, St. Louis, MO

INTERMISSION

4:10 Surgery for Congenital Heart Disease in Adults
James K. Kirklin, Birmingham, AL

Valve Selection for Valve Replacement

4:30 Mechanical Valves
Cary W. Akins, Boston, MA

4:50 Bioprosthetic Valves
William R. E. Jamieson, Vancouver, BC, Canada

5:10 Homograft Valves
Robert B. Karp, Chicago, IL

5:30–5:45 Panel Discussion: Questions and Answers

Session III: Pediatric Cardiac Surgery

2:00 Fontan Procedure: Techniques and Results With Tricuspid Atresia and Complex Single Ventricle
Gordon K. Danielson, Rochester, MN

2:20 The Arterial Switch Operation for Simple and Complex Forms of Transposition
Edward L. Bove, Ann Arbor, MI

2:40 Surgical Management and Results in Infants with Pulmonary Atresia With Intact Ventricular Septum
William G. Williams, Toronto, Ont, Canada

3:00 Surgical Management of Coarctation in Infants and Children
Ralph D. Siewers, Pittsburgh, PA

INTERMISSION

4:10 Aortic, Mitral, and Pulmonary Valve Repair in Infants and Children
Aldo R. Castaneda, Boston, MA

4:30 Repair of Truncus Arteriosus in Infants
Kevin Turley, San Francisco, CA

4:50 Surgical Management of Tetralogy of Fallot
Vaughn A. Starnes, Stanford, CA

5:10 Anomalous Origin of the Left Coronary Artery From the Pulmonary Artery
John W. Brown, Indianapolis, IN

Sunday, September 23, 1990

7:00–8:30 **The Premier Presentation of the STS National Database**
(No charge; registration requested)

7:00–8:30 **Introductory Session for Members and Guests**
A live demonstration of the National Database tracing its evolution and development through the comprehensive benefits it provides. A "walk through" the data entry forms, risk stratification system, data screens, and report capabilities with a focus on how the National Database can assist a cardiothoracic surgeon in his or her practice. Everyone welcome.

MORNING SCIENTIFIC PROGRAM

8:30–10:30 **PLENARY SESSION**

8:30 **Lung Transplantation**
Joel D. Cooper, St. Louis, MO

9:10 **Hypoplastic Left Heart Syndrome**
Moderator: Aldo R. Castaneda, Boston, MA

Surgical Repair
William I. Norwood, Jr, Philadelphia, PA

Cardiac Transplantation
Constantine Mavroudis, Chicago, IL

9:50 **Coronary Revascularization**

Angioplasty—Current Indications and Results
Spencer B. King, Atlanta, GA

Coronary Bypass—Current Indications and Results
Floyd D. Loop, Cleveland, OH

11:15–12:30 **THREE PARALLEL HOW-TO-DO-IT SESSIONS**

Session I: General Thoracic Surgery

11:15 Management of Infected Median Sternotomy Wounds
Geoffrey M. Graeber, Morgantown, WV

11:30 Intrathoracic Lung Cancer Staging
G. Alexander Patterson, Toronto, Ont, Canada

11:45 Sleeve Lobectomy
L. Penfield Faber, Chicago, IL

Noon Ivor-Lewis Esophagogastrectomy
Victor F. Trastek, Rochester, MN

12:15 Postpneumonectomy Empyema
Peter C. Pairolero, Rochester, MN

Session II: Adult Cardiac Surgery

11:15 Revascularization With the Gastroepiploic Artery
Bruce W. Lytle, Cleveland, OH

11:30 Retrograde Cardioplegia
W. Randolph Chitwood, Jr, Greenville, NC

11:45 Adult Homograft Aortic Valve Replacement: Surgical Challenges Requiring a Spectrum of Techniques for Solution
Richard A. Hopkins, Washington, DC

Noon Mitral Valve Repair—1990
Delos M. Cosgrove III, Cleveland, OH

Parallel How-to-Do-It Sessions, continued

12:15 Treatment of Aortic Dissection—Updated
E. Stanley Crawford, Houston, TX

Session III: Pediatric Cardiac Surgery

11:15 Postoperative Management of Pulmonary Hypertension in Infants and Children Including ECMO
James A. Alexander, Gainesville, FL

11:30 Atrioventricular Septal Defect Repair in Infancy
Frank M. Midgley, Washington, DC

11:45 What to Do If It Can't Be Fixed: Closed Palliative Procedures
Anthony L. Moulton, Omaha, NE

Noon Surgical Ablation of Arrhythmias in Children
David A. Ott, Houston, TX

12:15 Cryopreserved Allograft Valve Conduits and Vascular Tissue in the Repair of Complex Congenital Heart Disease
David R. Clarke, Denver, CO

12:30 ADJOURNMENT

GENERAL INFORMATION

Registration and Fees

An advance registration form with hotel reservation information will be mailed to Society members. Nonmembers should write to the Secretary, Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

Members and Candidate Members are not required to pay a registration fee for the general sessions. The fee for other physicians is $200, except guest speakers. Each resident will be charged $30 and will be required to present a letter from his or her chief of service to take advantage of this discounted fee. This letter can accompany an advance registration form or be presented at the time of on-site registration. If no letter accompanies the registration form, he or she will be charged the guest fee of $200. Nurses and paramedical personnel may register upon payment of a $30 registration fee and presentation of a letter of introduction from a Society member. The fee for the CPT-4 Coding Workshop held Saturday morning will be $90 per physician and $65 per nonphysician. There is no charge for the Sunday morning Premier Presentation of the STS National Database but advance registration is requested.

Accreditation

The Interim Meeting of The Society of Thoracic Surgeons is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. One credit hour in Category I of the Physician's Recognition Award of the American Medical Association may be claimed for each hour of participation by the individual physician.

1991 Annual Meeting of The Society of Thoracic Surgeons

The 1990 meeting is an Interim Meeting to be held at the Hyatt Regency Chicago in Chicago, Illinois, September 21–23, 1990. No abstracts are solicited for that program.

The Twenty-seventh Annual Meeting will be held at the San Francisco Moscone Center in San Francisco, California, February 18–20, 1991.

APPLICATION FOR MEMBERSHIP

(Deadline: September 1, 1990)

Requests for application forms for membership in The Society of Thoracic Surgeons should be addressed to James L. Cox, MD, Chairman, Membership Committee, The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

The completed application forms and supporting letters must be in the hands of the Membership Committee by **September 1, 1990**, for the applicant to be considered for election at the meeting in February 1991.

CALL FOR ABSTRACTS

(Deadline: September 12, 1990)

Abstracts for papers to be presented at the 1991 Annual Meeting are now being accepted. The deadline for receipt of abstracts is September 12, 1990. An original and one copy should be submitted, using the official Society abstract form (on verso of this page), to Alexander S. Geha, MD, and Robert A. Guyton, MD, Co-Chairmen, Program Committee (Abstracts), The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601. Additional forms are available upon request from The Society. Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. Abstracts must be in the hands of the Program Committee by **September 12, 1990.** Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

The Thoracic Surgery Directors Association (TSDA) has established a Resident Presentation Award for 1991. Potential TSDA Resident Award abstracts must represent original work by the resident, who is to be first author and presenter. TSDA Resident Award abstracts may be directed to the regular Scientific Session or the Research Forum.

Essayists are reminded that according to the bylaws of The Society, all papers accepted for presentation: (1) must be submitted in *triplicate* to the Secretary at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation; and (2) become the property of The Society if they are accepted for presentation.

It is well recognized that abstracts frequently belie their content by virtue of poor organization, and as a result valuable contributions to the Scientific Sessions may be unrecognized. It is important that methods and results be clearly defined in the abstract; therefore, general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Speakers for accepted papers are limited to ten minutes.

Instructions for Abstracts

The official abstract form printed on verso of this page and available from The Society, or photocopies thereof, must be used. **Authors must categorize the principal subject of their abstract by checking the appropriate box.**

If the author wishes to submit the abstract for consideration for the Thoracic Surgery Directors Association Award competition, the *additional* appropriate box must be checked. Also, the name of the Program Director must appear on a TSDA Resident Award abstract.

1. Full names of authors must appear on the abstract.
2. Institution or address is to be given, but omit titles, degrees, and appointments.
3. Abstracts must be limited to 250 words and must be typed double-spaced.
4. When percentages are used, the absolute numbers of derivation must be stated.
5. The body of the abstract should include:
   a. A brief statement of the purpose of the study being presented, with reference to the current state of research in the field.
   b. The methods of study or experimental approach clearly, but briefly, defined.
   c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
   d. A statement concerning the significance of the work and its possible implications for further research.
6. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

In discussion of papers, The Society encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of discussion in the form of "secondary papers" will not be welcomed.

CALL FOR SURGICAL FILMS OR VIDEO TAPES

(Deadline: September 1, 1990)

The popular surgical movie program will again be presented at the San Francisco meeting. The Program Committee hereby solicits the submission of surgical films, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to The Society. The film may not exceed ten minutes in length. Sound movies are acceptable but not necessary; however, live narration by the principal surgeon is a requirement for participation in the movie night program. The movies should be on 16-mm film or ¾-inch U-Matic video tape. The deadline for submission is **September 1, 1990.** Films and video tapes also should be sent to Alexander S. Geha, MD, and Robert A. Guyton, MD, Co-Chairmen, Program Committee, at The Society of Thoracic Surgeons, 111 E Wacker Dr, Chicago, IL 60601.

Richard P. Anderson, MD
Secretary

For Committee use only:

THE SOCIETY OF THORACIC SURGEONS

Abstract Form

For Committee use only:
Rating: (Highest 1)

1☐ 2☐ 3☐ 4☐ 5☐

LIMIT TO 250 WORDS AND DOUBLE-SPACE

TITLE

AUTHOR(S)

ADDRESS

PLEASE CHECK ONE APPROPRIATE CATEGORY

- ☐ **Pulmonary**
- ☐ **Esophagus**
- ☐ **Chest wall Mediastinum**
- ☐ **Trauma**
- ☐ **Transplantation**
- ☐ **Heart**
- ☐ **Great vessels**
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- ☐ **Congenital**
- ☐ **Coronary**
- ☐ **Electrophysiology**
- ☐ **Myocardial protection**
- ☐ **Extracorporeal circulation**
- ☐ **Endoscopy**
- ☐ **Vascular surgery**
- ☐ **Research, Cardiac**
- ☐ **Research, Congenital Cardiac**
- ☐ **Research, Transplantation**
- ☐ **Research, General Thoracic**

☐ **PLEASE CHECK IF ALSO SUBMITTED FOR THE THORACIC SURGERY DIRECTORS ASSOCIATION AWARD**

Program Director's Name:

____

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I acknowledge that the material will not be presented elsewhere if accepted for presentation on The Society of Thoracic Surgeons Scientific Program. I further understand that the Editorial Board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

____
Signature of Senior Author

Information About Membership in The Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) is the largest organization of its kind devoted primarily to the practice of thoracic and cardiovascular surgery. The major purpose of The Society is educational, with the aim of providing thoracic and cardiovascular surgeons from both academic and private practice environments a forum for presentation and discussion of scientific topics. As outlined in the original bylaws of The Society, this educational emphasis is designed to accomplish the broader goal of improving the quality and practice of thoracic and cardiovascular surgery as a specialty.

The STS recently celebrated its 25th Anniversary, having been founded in 1964. Since its inception, The Society has grown continually so that at present the membership includes the majority of board certified thoracic surgeons in the United States as well as thoracic and cardiovascular surgeons from 45 other countries.

In addition to an annual scientific meeting, the STS has more than 20 committees working on diverse matters related to improving thoracic and cardiovascular surgery as a specialty. Examples of these committees are: Standards and Ethics, Government Relations, Medico-Legal Affairs, Surgical Standby for PTCA, Physician Reimbursement, CPT-4 Advisory, Education and Resources, and Cardiothoracic Surgical Practice Guidelines. The Committee to Analyze Circulatory Assist Devices and Artificial Hearts sponsors topical meetings (next meeting, November 15–17, 1991, in San Francisco). The Committee to Develop a National Database for Thoracic Surgery plans to implement the first comprehensive database program for thoracic and cardiovascular surgeons in the United States; it will be offered to members in the near future.

There are five types of membership in The Society of Thoracic Surgeons: active, senior, honorary, international, and candidate.

Active Member Applicants for active membership must be surgeons whose practice is devoted primarily to the field of thoracic and cardiovascular surgery.

QUALIFICATIONS: Applicants must be Diplomates of the American Board of Thoracic Surgery or Fellows in The Royal College of Surgeons of Canada, and be established in the practice of thoracic and/or cardiovascular surgery for a minimum of three years. There must be sponsoring letters from three active STS members.

Senior Member Any active member or international member, upon reaching the age of sixty-five years, shall automatically become a Senior Member.

Honorary Member Honorary Membership shall be reserved for distinguished persons worldwide who have achieved prominence in the field of thoracic and cardiovascular surgery and have contributed to its advancement. Honorary members shall be elected by a majority vote of The Society at its annual business session upon recommendation of the Council of the STS.

International Member Members from countries other than the United States and Canada were previously accepted only as active members. Because of differences in training and practice, the application process for foreign members was often complex and time consuming. To allow for greater participation by thoracic and cardiovascular surgeons from other countries, the bylaws have been revised to provide for a category of International Member, which is the category for all members outside the United States and Canada.

QUALIFICATIONS: Applicants shall reside outside the United States and Canada. Their training in this specialty shall be considered equivalent to that of Active Members. They shall have achieved appropriate certification or recognition of achievements in this specialty in their country and must devote the majority of their professional efforts to the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee.

Candidate Member Candidate membership was created to allow participation of younger surgeons in the time prior to being qualified for active membership.

QUALIFICATIONS: Applicants shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a similar program approved for training by The Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in process of acquiring certification by the American Board of Thoracic Surgery or The Royal College of Surgeons of Canada are eligible for this type of membership.

If you would like to receive an application for membership in The Society, send the request printed below. This year's deadline for receipt of applications is September 1, 1990. We suggest you apply soon as it takes time to process the application. Approved applications will be presented to the membership at the February 1991 Annual Meeting in San Francisco.

REQUEST FOR APPLICATIONS

Please send an application for: ☐ Active membership ☐ International membership ☐ Candidate membership

TO: NAME: ____________________

ADDRESS: ____________________

____

TELEPHONE NUMBER: ____________________

Send to: James L. Cox, MD, Chairman, Membership Committee
The Society of Thoracic Surgeons, 111 East Wacker Drive, Suite 600, Chicago, IL 60601
Telephone: (312) 644-6610; FAX: (312) 938-1214

THE ANNALS OF THORACIC SURGERY
Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

Myocardial Preservation Into the 21st Century, Oxford, England—August 12–15, 1990

For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Drive, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870 (facsimile: (714) 759-6911).

Thirty-ninth Annual Meeting of the Scandanavian Association for Thoracic and Cardiovascular Surgery and the Scandanavian Society for Extracorporeal Technology, Reykjavík, Iceland—August 29–31, 1990

For information on this meeting, contact G. Ólafsson, MD, Chairman, Department of Thoracic and Cardiovascular Surgery, Landspítalinn, University Hospital, Reykjavík, Iceland.

Thirty-ninth Congress of the European Society for Cardiovascular Surgery, Budapest, Hungary—September 9–12, 1990

For information on this meeting, contact Budapest Convention Centre, H-1444, PO Box 233, Budapest XI, Jagello u 1-3, Hungary; or telephone (361) 852-507 (facsimile: (361) 665-636; telex: 22-7717).

Fourth Annual Meeting of the European Association for Cardio-thoracic Surgery, Naples, Italy—September 17–19, 1990

For information on this meeting, contact the Organizing Secretariat, MCM, Rione Sirignano, 5, 80121 Naples, Italy; or telephone (0)81/7611085-7611277 (facsimile: (0)81/664372; telex: 710626).

Second Annual Meeting of the International Society for Applied Cardiovascular Biology, Venice Lido, Italy—September 17–20, 1990

For information on this meeting, contact the Congress Secretariat, Kele Teo, San Marco 4930, Venice, Italy.

Interim Meeting of The Society of Thoracic Surgeons, Chicago, Illinois—September 21–23, 1990

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

Mechanical Circulatory Support 1990, London, England—September 26–28, 1990

For information on this meeting, contact Anne Sumner, Mechanical Circulatory Support 1990, Medical Research Services, 60 Oxford St, Southampton SO1 1DL, Hants, England; or telephone 0703 231068.

Controversies in Cardiovascular Disease: Surgical Versus Medical Treatment, Aalst, Belgium—September 28–29, 1990

For information on this meeting, contact Dr F. Wellens, Department of Cardiovascular Surgery, O.L. Vrouwziekenhuis, Moorselbaan 164, B-9300 Aalst, Belgium; or telephone 053/78 53 53 (facsimile: 053/78 38 76).

American College of Surgeons, San Francisco, California—October 7–12, 1990

For information on this meeting contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-sixth Annual Scientific Assembly, American College of Chest Physicians, Toronto, Ontario, Canada—October 22–26, 1990

This meeting is sponsored by the American College of Chest Physicians and the International Academy of Chest Physicians and Surgeons. For information, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association, Cerromar Beach, Puerto Rico—November 8–10, 1990

For information on this meeting, contact Gordon F. Murray, MD, Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610 (facsimile: (312) 938-1214).

Sixty-third Scientific Session of the American Heart Association, Dallas, Texas—November 12–15, 1990

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 750-5300.

Global Plenum on Organ Transplantation, Lucknow, India—December 14–16, 1990

For information on this meeting, contact Prof Probal Ghosh, Plenum Secretariat, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Rd, Post Box 375, Lucknow 226001, India.

Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons, San Francisco, California—February 17–20, 1991

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

CLASSIFIED ADS

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Media for Medicine, Inc, 440 Park Avenue South, New York, NY 10016 (telephone: (212) 684-5540; facsimile: (212) 545-0651). All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.10 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $15.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad orders should be for a maximum of 6 months; ads may be renewed for up to 6 months at a time. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3695). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the ad. To respond to an anonymous ad, write to Box Number, *The Annals of Thoracic Surgery*, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Associate Director for Heart Transplantation is urgently needed for rapidly expanding heart transplantation program in California.

Please respond with curriculum vitae to the Pacific Cardiothoracic Surgery Group, 201 S Alvarado St, Suite 626, Los Angeles, CA 90057. 240L/K

Cardiovascular and thoracic surgeon, board eligible/certified, wanted to join well-established private practice located in Ft. Lauderdale, FL. Send CV.

Please respond to Box 251. 251L/K

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to Box 252. 252G/L

Cardiothoracic/vascular surgeon wanted to join established practice in Ohio. Recent graduate preferred. Please submit curriculum vitae and three references.

Please respond to Box 302. 302C/I

Cardiac surgeon wanted to join established private practice in Eastern PA. Primarily adult cardiac. BC/BE required. Please send CV.

Please respond to Box 315. 315D/I

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another physician in private practice in Northeast. Immediate availability. Please respond with curriculum vitae.

Please respond to Box 316. 316D/I

Excellent opportunity for recent graduate, board eligible or certified, for private practice of cardiac, thoracic, and major vascular cases in Great Lakes area. Include references and curriculum vitae.

Please respond to Box 335. 335E/J

Cardiothoracic surgeon needed for expanding program in mid-Michigan. Primarily adult cardiac and thoracic. BC/BE required. Please send CV with references.

Please respond to Box 337. 337E/J

Cardiothoracic surgeon wanted for busy, expanding Southeastern private group in regional medical center with university affiliation. Practice includes most aspects of adult and pediatric cardiac and thoracic surgery. Surgeon must be board eligible or certified with contemporary training. Excellent opportunity for suitable applicant.

Please respond to Box 342. 342F/I

Thoracic surgery residency: Residency in thoracic surgery. Position available July 1991 at the University of Massachusetts Medical School/Hospital. Three-year program includes training in adult and pediatric cardiac and general thoracic surgery.

Interested candidates may contact Thomas J. Vander Salm, MD, Department of Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655. 347F/H

Cardiovascular and thoracic surgeon: Excellent opportunity to join a busy north central Florida group. Practice specializes in adult cardiac and thoracic surgery. Excellent benefit package. Please reply with curriculum vitae.

Please respond to Box 348. 348F/K

Cardiovascular and thoracic surgeon, BE/BC, to join in 2-man private practice in cardiovascular and thoracic surgery in the Northeast. Excellent benefits package. Association will lead to partnership. Please send curriculum vitae.

Please reply to Box 350. 350F/K

Assistant surgeon sought for busy adult cardiothoracic surgery practice. Entire responsibility will be to assist 4 senior surgeons in the operating room. Board certification or eligibility in general surgery and some experience in vascular and/or thoracic surgery helpful, though not essential. Generous salary and fringes. Position is available immediately and could be permanent. Ideal location in very pleasant, small city near major eastern metropolitan centers.

Please respond to Lawrence I. Bonchek, MD, 555 North Duke St, Lancaster, PA 17603; (717) 295-8395. 352G/H

Cardiothoracic surgeon needed for established program in scenic Montana Unique opportunity for congenial private practice lifestyle combined with high-tech hospital environment including dedicated cardiac OR, cardiac anesthesia, and cardiac intensive care unit. Solo practice or association leading to partnership. Could be experienced surgeon or recent graduate from quality program.

Please respond to Box 354. 354G/L

BC/BE general/thoracic surgeon—California: We need a general surgeon who is also trained in thoracic surgery and interested in an excellent practice doing general and thoracic surgery (no open heart). We offer the opportunity to establish your own private practice with no investment, guaranteed income. Well-equipped 112-bed full-service hospital. A growing area with new businesses and stable economy. Our service area population is now 90,000. Located in central California near Sequoia National Park. Tulare offers an excellent family-oriented lifestyle with all expected amenities. Beautiful homes, located close to hospital and office, are affordably priced. Good schools, many community activities and abundant recreation including golf, tennis, skiing, mountain and equestrian activities. Easy access to all California's major metropolitan and resort areas.

Please contact Tulare District Hospital Physician Recruiting Office, PO Box 90112, Los Angeles, CA 90009; (800) 468-2687. 355G/H

Thoracic surgeon wanted: A busy thoracic practice 20 miles south of Boston seeks to add a third surgeon by July 1991. Candidate must be board certified or eligible. This active practice operates from a multihospital referral base. The community is an ideal area for family living, with excellent schools and nearby Boston and Cape Cod cultural and recreational facilities. Competitive salary, malpractice insurance, and excellent benefit package. Please respond with CV.

Please respond to Box 356. 356G/L

Cardiovascular and thoracic surgeon: Position available for a BC/BE surgeon to join expanding surgical practice associated with highly trained invasive cardiologists and cardiac anesthesiologists in Ocala, Florida. (Ocala is located in the center of Florida, 75 miles north of Orlando.) Excellent benefits package, including great location for family activities. Recent graduates considered.

Please send a curriculum vitae to Wayne McGraw, Executive Director, Ocala Heart Institute, PO Drawer 3130, Ocala, FL 32678. 357G/I

Cardiovascular and thoracic surgeon—board eligible or qualified—wanted to join 4 physicians in very active private practice in greater Chicago area. Respond with curriculum vitae.

Please respond to Box 359. 359G/H

Cardiothoracic and vascular surgeon, board eligible/certified with experience in adult cardiac thoracic and vascular surgery, wanted to join well-established practice located in southern California. Send CV and references.

Please respond to Box 361. 361G/H

Cardiovascular/thoracic surgeon, BC/BE, to join well-established private practice on Florida west coast. Expertise in adult cardiac, vascular, and thoracic surgery required. Recent graduate with transplant experience preferred. Excellent compensation and benefits leading to full partnership. Please include curriculum vitae and references with response.

Please respond to Box 363. 363G/J

Cardiovascular-thoracic surgeon, BC/BE, needed to join busy expanding private practice in the Midwest. Excellent program, large number of experienced cardiologists. Initial contact should include curriculum vitae and references. Ideal candidate will have results to submit.

Please respond to Box 365. 365H

Cardiothoracic surgeon, BE/BC, to join established 1-man private practice involved with adult cardiac, thoracic, and vascular surgery in major Midwest community. New or recent graduate preferred. Salary leading to partnership. Please send CV, clinical experience, and references.

Please respond to Box 366. 366H/K

Vascular surgeon, board certified/board eligible, recently trained, wanted to join a busy solo vascular surgeon in north central West Virginia using 300-bed very progressive hospital. Excellent package and potential.

Please respond to Box 367. 367H/K

Cardiovascular and thoracic surgeon, board certified or board eligible, wanted for an established private practice of cardiac, thoracic, and vascular surgery in the Southeast with potential university affiliation. Initial contact should include curriculum vitae, clinical experience in all three disciplines, surgical results, and references.

Please respond to Box 368. 368H/J

Cardiac surgeon, board certified or board eligible, for very busy private practice group doing primarily adult cardiac and vascular surgery. Seeking an Associate to join well-established practice in northeast Ohio metropolitan area. Please respond with curriculum vitae and references.

Please respond to Box 370. 370H/A

Thoracic surgeon for rapidly growing group practice in the NYC area. Excellent salary. Please respond with CV and references.

Please respond to Box 372. 372H/I

Cardiothoracic and vascular surgeon, board eligible/certified with experience in adult cardiac thoracic and vascular surgery, wanted to join well-established practice located in southern California. Send CV and references.

Please respond to Box 373. 373H/I

Cardiovascular surgeon: We are looking for a recently trained B/E or B/C CV surgeon to join our very busy and enjoyable 2-man cardiovascular department at The Billings Clinic, a progressive major regional multispecialty clinic in the northern Rocky Mountain region. This is an outstanding practice opportunity for the right individual seeking a challenging and rewarding surgical practice in surroundings conducive to the highest quality of living for the surgeon and his or her family.

For further information, please call or send CV to Hewes D. Agnew, MD, or J. Scott Millikan, MD, The Billings Clinic, PO Box 35100, Billings, MT 59107-5100; (406) 256-2500. 375H/J

Thoracic surgeon, BC/BE, needed to join two others in a busy thoracic surgical practice without open heart surgery. Located in a prime suburb of NYC with a good quality of life. Rapid partnership advancement. Recent graduate preferred. Please reply with a curriculum vitae.

Please respond to Box 376. 376H/J

Cardiovascular surgeon wanted to join busy private practice in excellent Florida location. Practice includes all aspects of adult cardiovascular and thoracic surgery. Would prefer a recent graduate. Send curriculum vitae.

Please respond to Box 377. 377H/J

Busy, established, university-affiliated, noncardiac thoracic surgical group in private practice in Northeast. Excellent salary and benefits leading to partnership. ABTS qualified or certified.

Please respond to Box 378. 378H

Recently trained, board certified or eligible thoracic and cardiovascular surgeon needed to join established surgical practice in beautiful wooded deep east Texas. Charming university community. Diversified practice of pulmonary, vascular, and cardiac surgery. No pediatric open heart surgeries.

Please respond to Box 379. 379H

Cardiovascular and thoracic surgeon, BC/BE, to join established group doing high volume adult cardiac and thoracic surgery in major teaching hospital, with medical school affiliation, in New York City. Please respond with curriculum vitae.

Please respond to Box 381. 381H

Cardiovascular/thoracic surgeon to complete 3-man group in adult cardiothoracic private practice in Michigan. Must be board eligible or certified. References required.

Please respond to Box 382. 382H/J

We are seeking cardiothoracic candidates for either Assistant or Associate Professor of Surgery. Applicants should have experience in surgical research and/or teaching. Applicant should be technically strong in all phases of adult cardiac surgery. Additional experience in pediatric cardiac surgery would be helpful as an extra qualification.

Please send applications to W. Randolph Chitwood, Jr, MD, Professor and Chief, Division of Cardiac Surgery, Department of Surgery, East Carolina University School of Medicine, Greenville, NC 27858-4354. Federal law requires proper documentation of identity and employability prior to final consideration for this position. East Carolina University is an equal opportunity/affirmative action employer. 383H/I

Cardiothoracic surgery group seeking an additional board eligible/board certified surgeon with interests and skills in general thoracic surgery for busy expanding practice. Private 3-man group practices in the Southeast in university-affiliated regional medical center. Practice currently includes mainly adult and pediatric cardiac and pulmonary surgery. Excellent opportunity for suitable applicant.

Please respond to Box 384. 384H/K

SITUATIONS WANTED

Cardiovascular and thoracic surgeon, 41, University trained, wishes to relocate. ABS and ABTS certified, member of the STS, ICS, ISHT, ACC, and AHA. Author of several publications. Currently experienced in IMA surgery, valve repair and replacement. Ten years ago developed a successful and busy pediatric cardiac surgery program, with extensive experience in neonates and infants.

Please respond to Box 343. 343F/H

Cardiothoracic surgeon, 36, 2 years' experience in adult cardiac surgery. Excellent results. Wishes to relocate to West Coast or the Northwest.

Please respond to Box 369. 369H/J

Thoracic and cardiovascular surgeon, board certified, with broad experience in all phases of the specialty except transplantation wishes to relocate. Curriculum vitae and references on request.

Please respond to Box 371. 371H/I

Two board-certified experienced clinical cardiovascular perfusionists are seeking to join a professional private cardiovascular surgical group or private cardiovascular surgeon.

Please respond to Box 374. 374H

FELLOWSHIPS

Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite 312, Sacramento, CA 95819. 364G/L

Fellowship in cardiovascular surgery available immediately with group doing high volume adult cardiac procedures in major teaching hospital with medical school affiliation in New York City. Ideal for person desiring 1 year between training or general surgical resident awaiting CT residency. Please respond with curriculum vitae.

Please respond to Box 380. 380H

CARDIOVASCULAR SURGEON NEEDED FOR PORTLAND, OREGON

Five man cardiovascular surgical team with an active, expanding practice in the Pacific Northwest has an immediate opening for a Board Certified/Board Eligible Cardiovascular Surgeon. Large volume cardiac surgery program drawing referrals for broad geographic area. Opportunity to conduct clinical research in a private practice setting.

For further information about this exceptional private practice opportunity, please send a CV to:

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Cardiothoracic Fellow

The Lankenau Hospital and Medical Research Center are state-of-the-art medical teaching and research facilities nestled in a beautiful, yet convenient suburban Philadelphia location. This past year we performed over 650 open heart surgeries.

We currently have a position to start immediately. We also have a position available July 1, 1991 on our staff for a Cardiothoracic Surgical Fellow. The ideal candidate should be board eligible or certified in general surgery. Board eligible in thoracic surgery highly desired. A Pennsylvania license is a must. Clinical Fellows are welcome to apply.

Along with top of the line technology and professional colleagues, the positions offer medical benefits, no city wage tax deducted and a non-smoking environment. For further information, please contact **Dr. Scott M. Goldman, c/o Personnel Department.**

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The Medical Staff and Administration of Conemaugh Valley Memorial Hospital, a 405-bed major teaching, University-affiliated, regional medical center with level I trauma and helicopter services, seek a leading cardiovascular surgeon to develop a premier open-heart program at our institution. The successful candidate must lend instantaneous credibility to this new program through current recognition as an outstanding clinician. New facilities, an active invasive interventional cardiology program and a free hand in program development await the Director. Clinical and financial success are essentially guaranteed. For additional information regarding this outstanding opportunity in our forward-looking institution and extremely livable community, please contact: **Kenneth W. Rowe Jr., M.D., Senior Vice President, Medical Affairs, 814-533-9721.**

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Baylor College of Medicine

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Rafael Espada, Program Director 713-790-4556

Royal Brompton and National Heart Hospital

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This is an excellent opportunity for senior trainees to spend a year in this historic London establishment. There is wide exposure to all aspects of cardiothoracic surgical practice, including transplantation, paediatric, electrophysiology as well as a broad spectrum of pulmonary and oesophageal disease. There is close liaison with the National Heart and Lung Institute for those wishing to participate in research. Positions are available from February 1991.

Please send curriculum vitae to Ms J. Simkins, Royal Brompton and National Heart Hospital, Fulham Road, London SW3 6HP, England.

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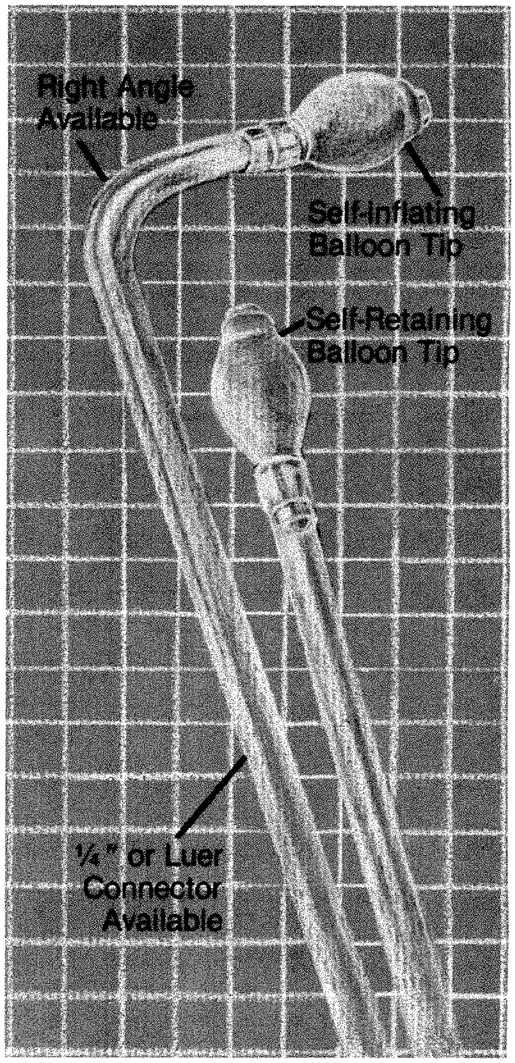
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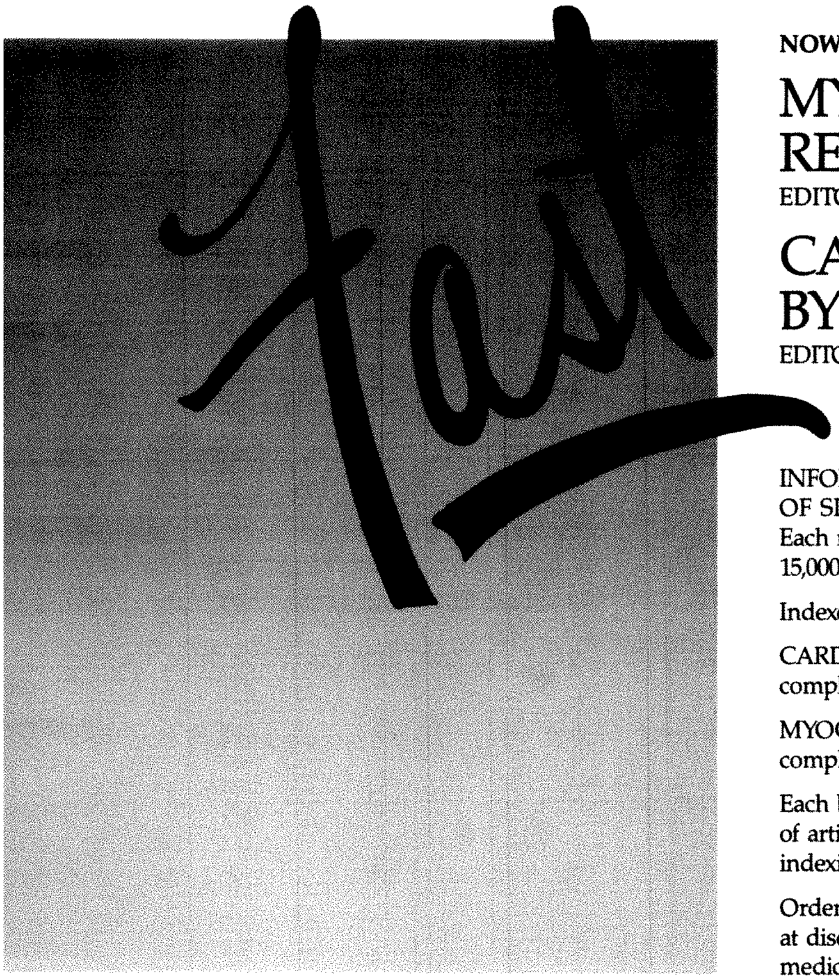

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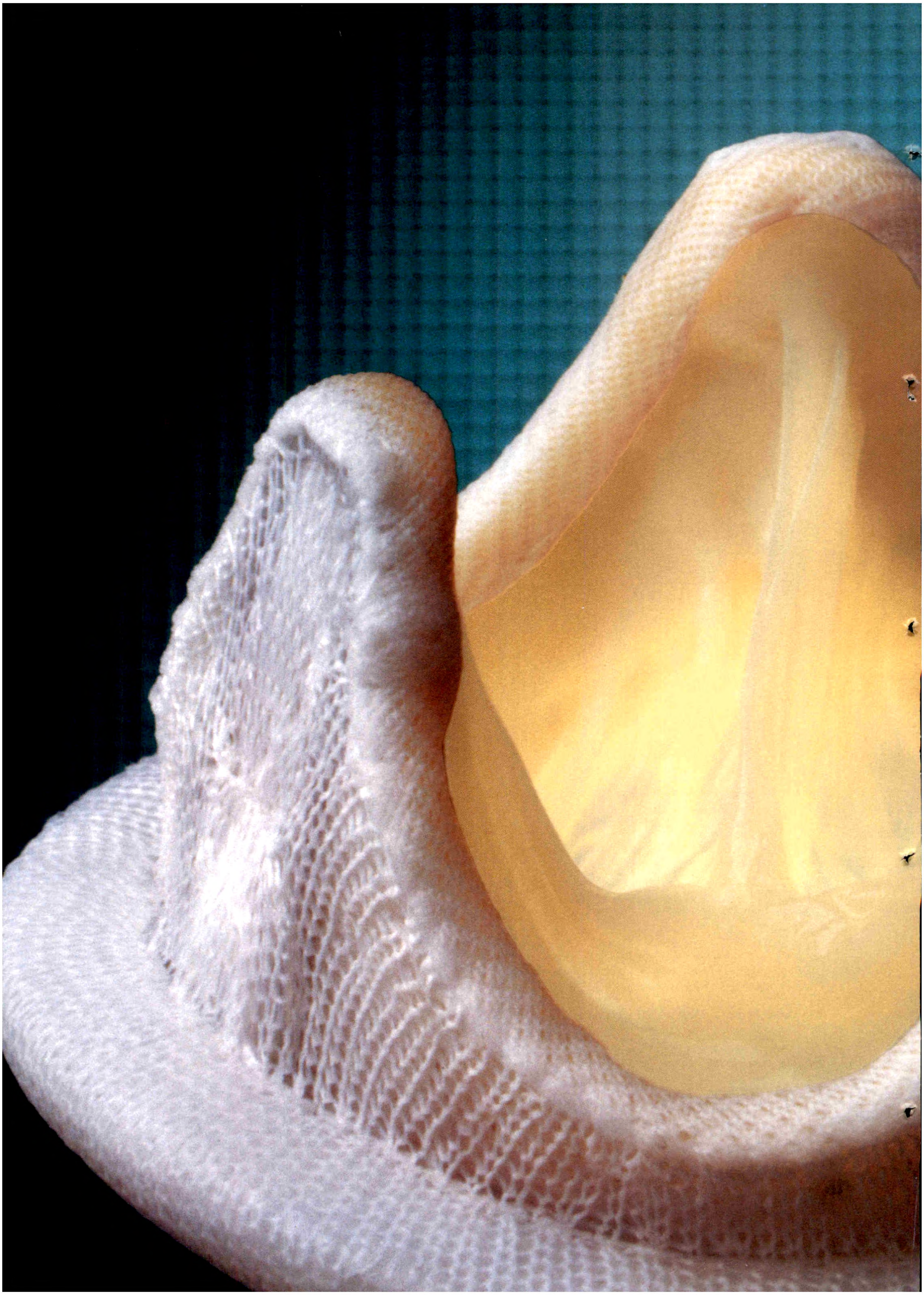

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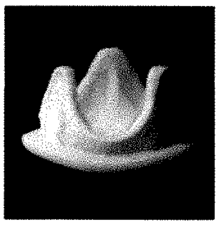

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The Carpentier-Edwards bioprosthesis is intended for use in patients whose aortic or mitral valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic or mitral valve prosthesis which is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. **Warnings:** For Single Patient Use Only In the presence of conditions affecting calcium metabolism or when calcium-containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients under 20 years of age, in patients on a high calcium diet, in the presence of severe systemic hypertension, and in patients who are on maintenance hemodialysis. The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Caréful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed.Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile**. The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions: 1.** When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Carpentier-Edwards bioprostheses to calcification as compared to other commercially available porcine valves. **Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician. Baxter International Inc. is the owner of the following US patent which covers the products described herein: 4,106,129. Patent numbers in foreign countries supplied upon request. See package insert accompanying product for a full discussion of warnings, contraindications, complications and prescribing information. Carpentier-Edwards® is a registered trademark of Baxter International Inc.

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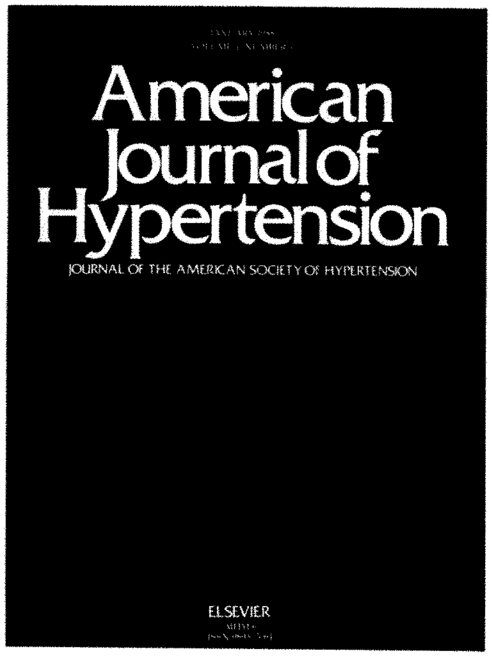
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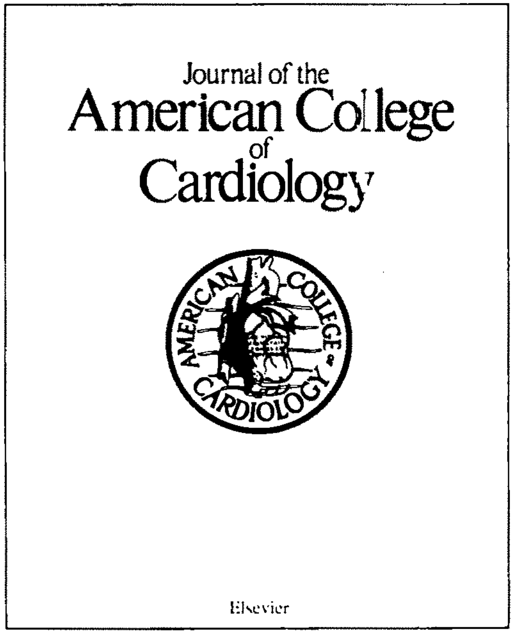

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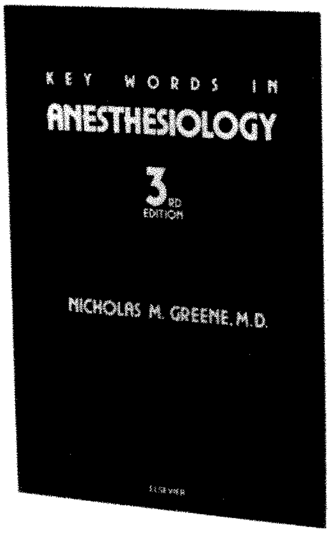

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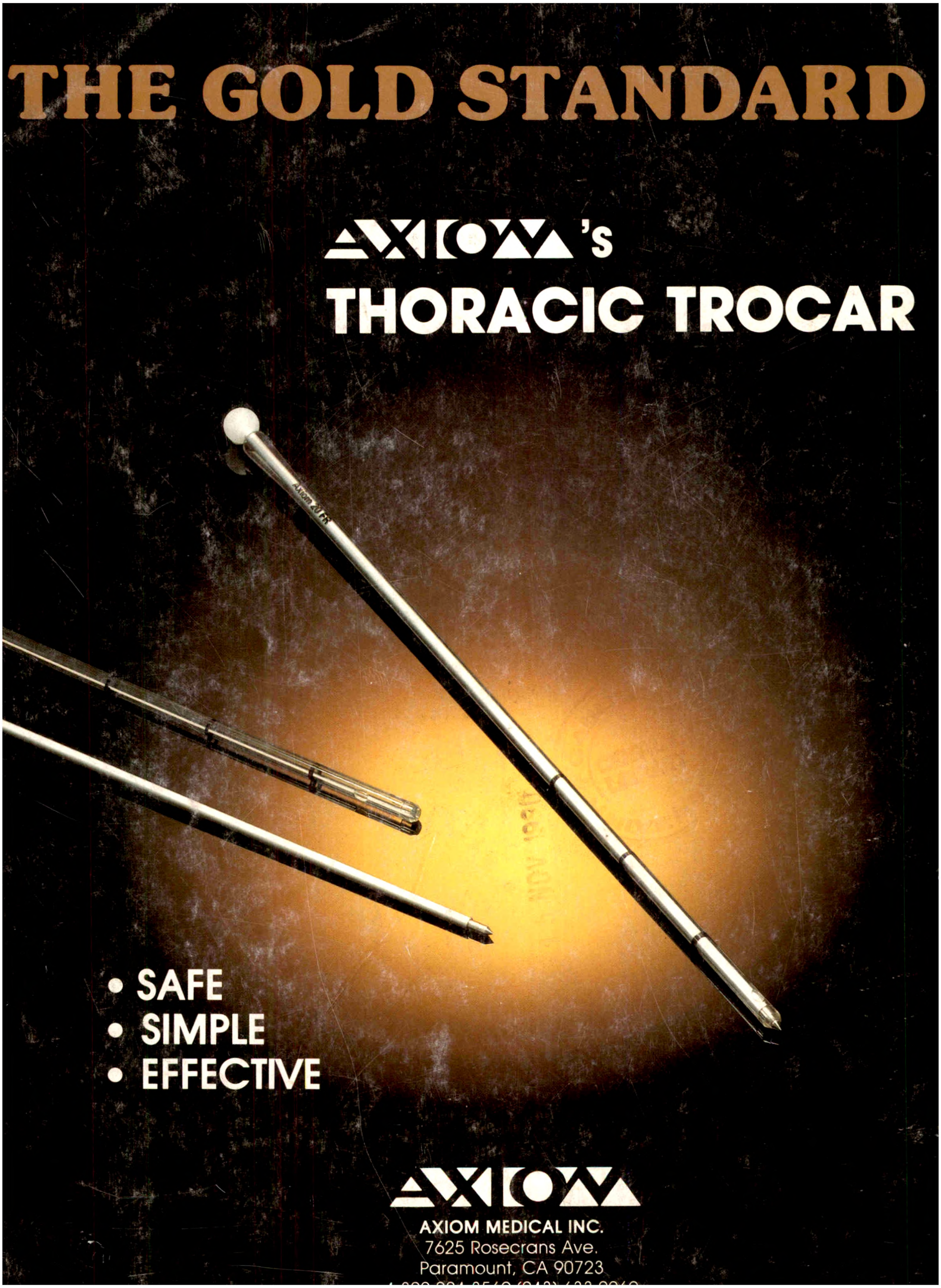

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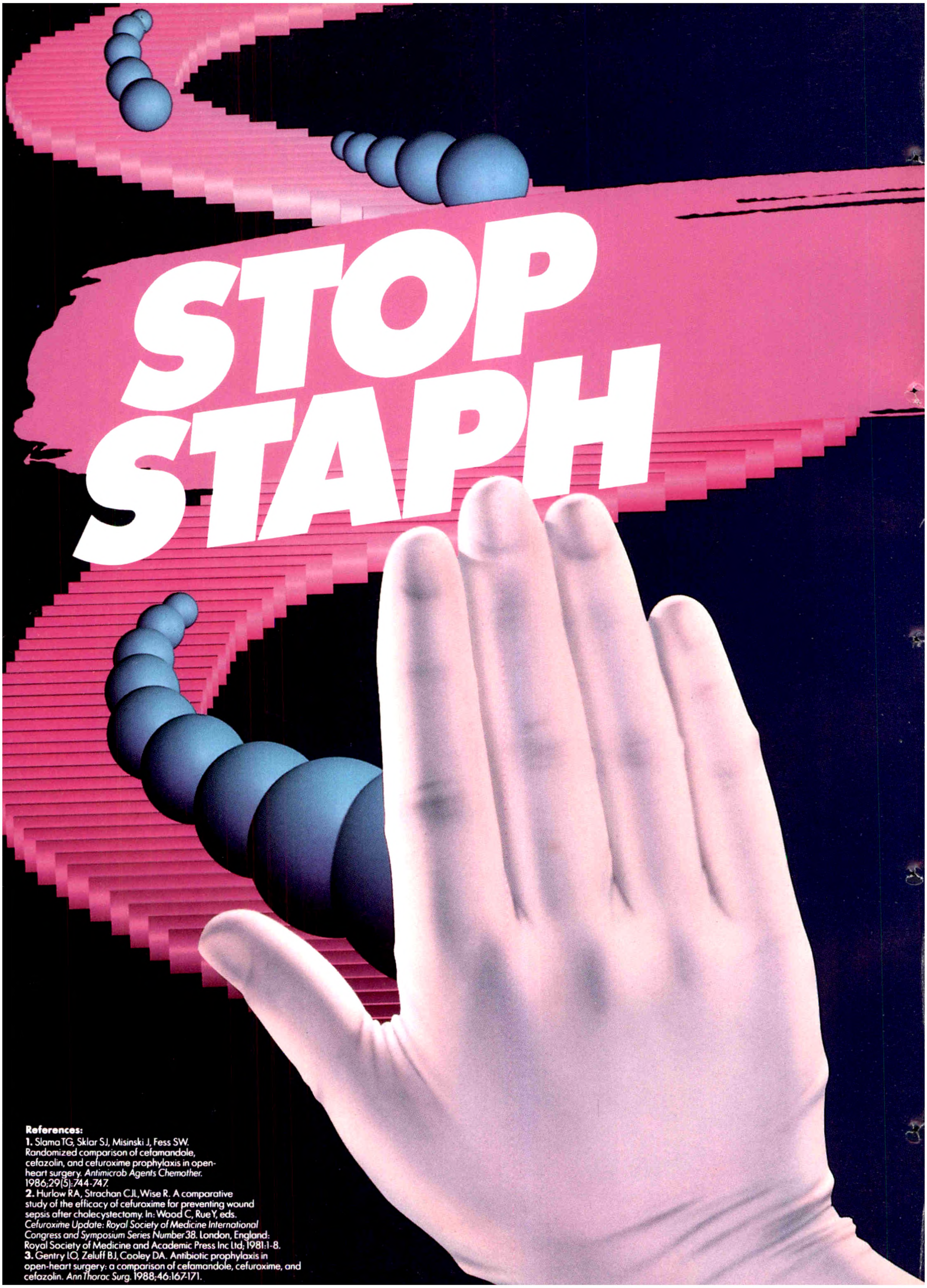

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INDICATIONS AND USAGE: Zinacef® is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases.

1. **Lower Respiratory Tract Infections,** including pneumonia, caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), *Haemophilus influenzae* (including ampicillin-resistant strains), *Klebsiella* spp, *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pyogenes*, and *Escherichia coli*.
2. **Urinary Tract Infections** caused by *E coli* and *Klebsiella* spp.
3. **Skin and Skin Structure Infections** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, *E coli*, *Klebsiella* spp, and *Enterobacter* spp.
4. **Septicemia** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pneumoniae*, *E coli*, *H influenzae* (including ampicillin-resistant strains), and *Klebsiella* spp.
5. **Meningitis** caused by *S pneumoniae*, *H influenzae* (including ampicillin-resistant strains), *Neisseria meningitidis*, and *S aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea:** Uncomplicated and disseminated gonococcal infections due to *Neisseria gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *S aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. Zinacef has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to Zinacef.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, Zinacef may be used concomitantly with an aminoglycoside (see PRECAUTIONS). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The preoperative prophylactic administration of Zinacef may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (eg, vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. Zinacef should usually be given one-half to one hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of Zinacef has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that Zinacef therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: Zinacef® is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF® IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although Zinacef® rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Zinacef should be reduced in patients with transient or persistent renal insufficiency (see DOSAGE AND ADMINISTRATION), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Zinacef may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest® tablets), but not with enzyme-based tests for glycosuria (eg, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Zinacef.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since Zinacef is excreted in human milk, caution should be exercised when Zinacef is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: Zinacef® is generally well tolerated. The most common adverse effects have been local reactions following intravenous administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with intravenous administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in less than 1% of the patients treated with Zinacef and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in less than 1 in 250 patients and, as with other cephalosporins, rare cases of anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (less than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence were seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics.

Adverse Reactions: Toxic epidermal necrolysis, fever, vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see DOSAGE AND ADMINISTRATION). If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Prolonged prothrombin time, pancytopenia, agranulocytosis, thrombocytopenia.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zinacef® product labeling.)

Impaired Renal Function: A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 1 in product package insert).

HOW SUPPLIED: Zinacef® in the dry state should be stored between 15° and 30°C (59° and 86°F) and protected from light. Zinacef is a dry, white to off-white powder supplied in vials and infusion packs as follows:

NDC 0173-0352-31	750-mg* Vial (Tray of 25)
NDC 0173-0354-35	1.5-g* Vial (Tray of 25)
NDC 0173-0353-32	750-mg* Infusion Pack (Tray of 10)
NDC 0173-0356-32	1.5-g* Infusion Pack (Tray of 10)
NDC 0173-0400-00	7.5-g* Pharmacy Bulk Package (Tray of 6)

Zinacef frozen as a premixed solution of cefuroxime sodium should not be stored above -20°C. Zinacef is supplied frozen in 50-ml, single-dose, plastic containers as follows:

NDC 0173-0424-00	750-mg* Plastic Container (Carton of 24)
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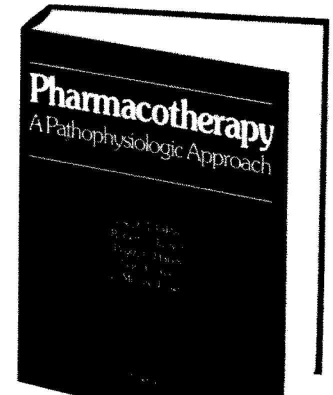

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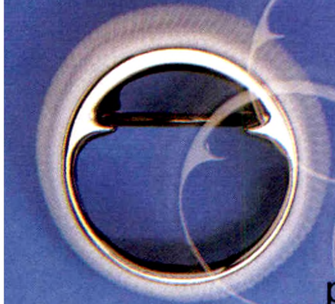
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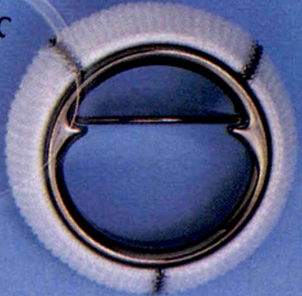
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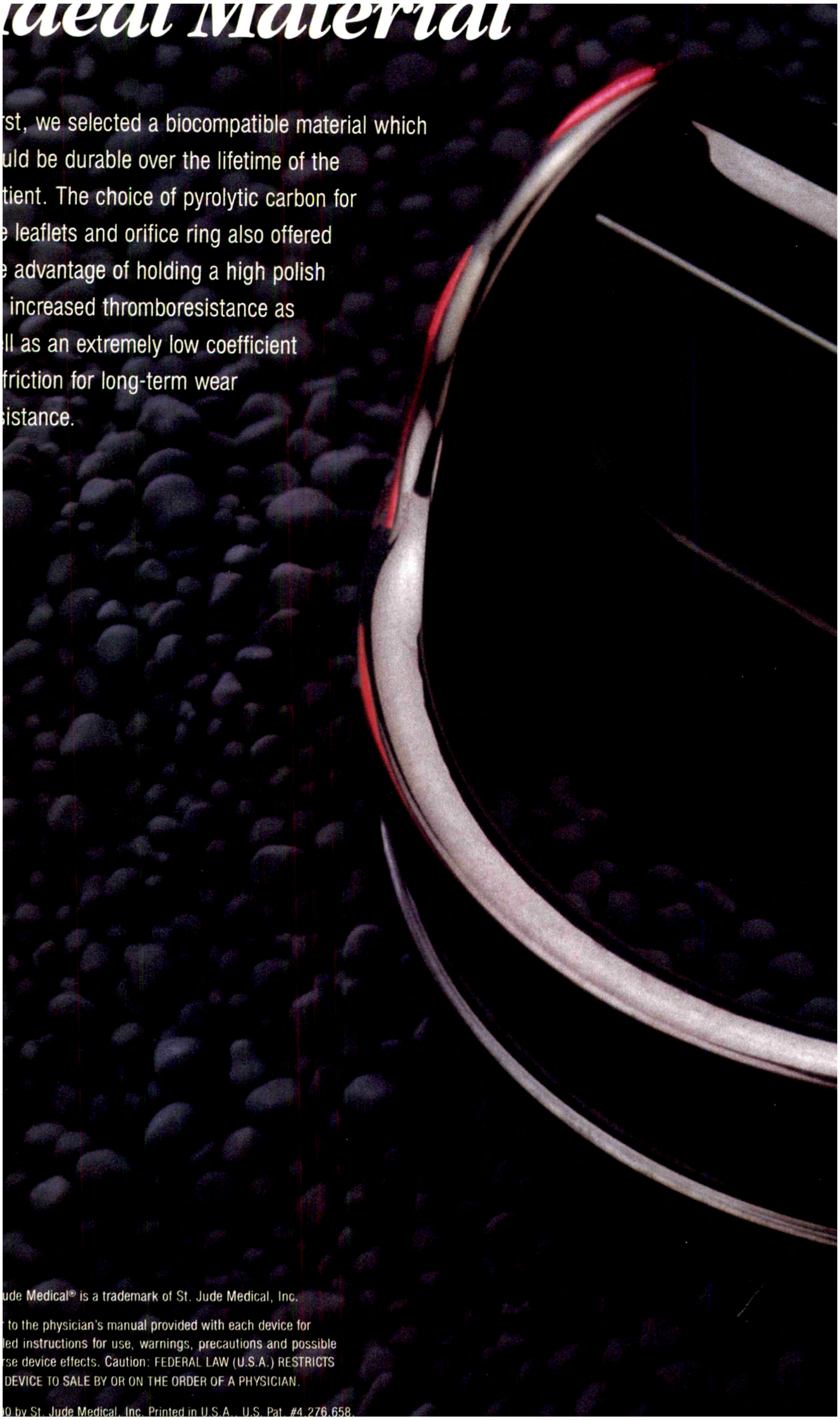

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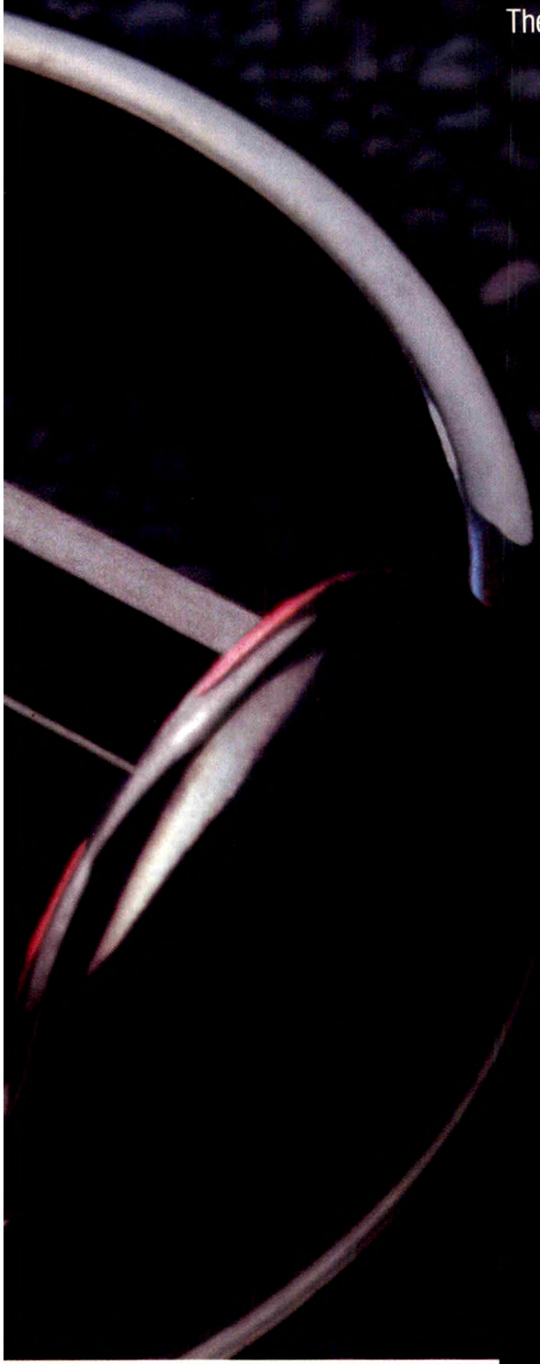

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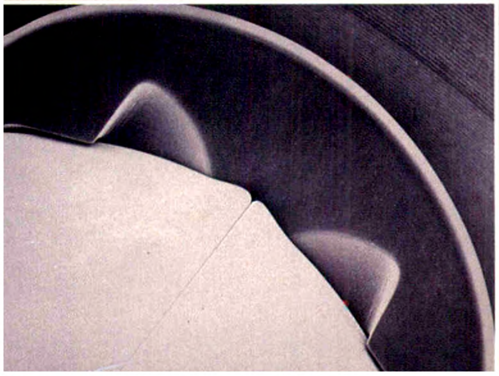

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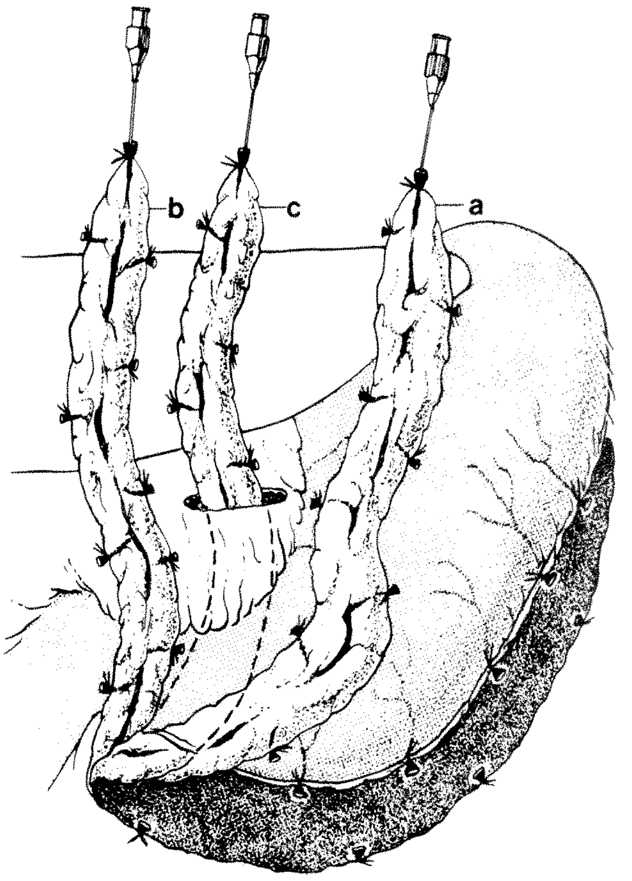

Figure 4. *Routes of the right gastroepiploic graft to the diaphragm are:* **(A)** *anterior to the stomach (rare),* **(B)** *anterior to the duodenum, and* **(C)** *posterior to the stomach through the avascular space in the lesser sac (most common).*

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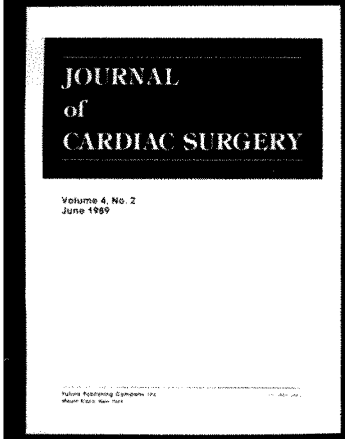

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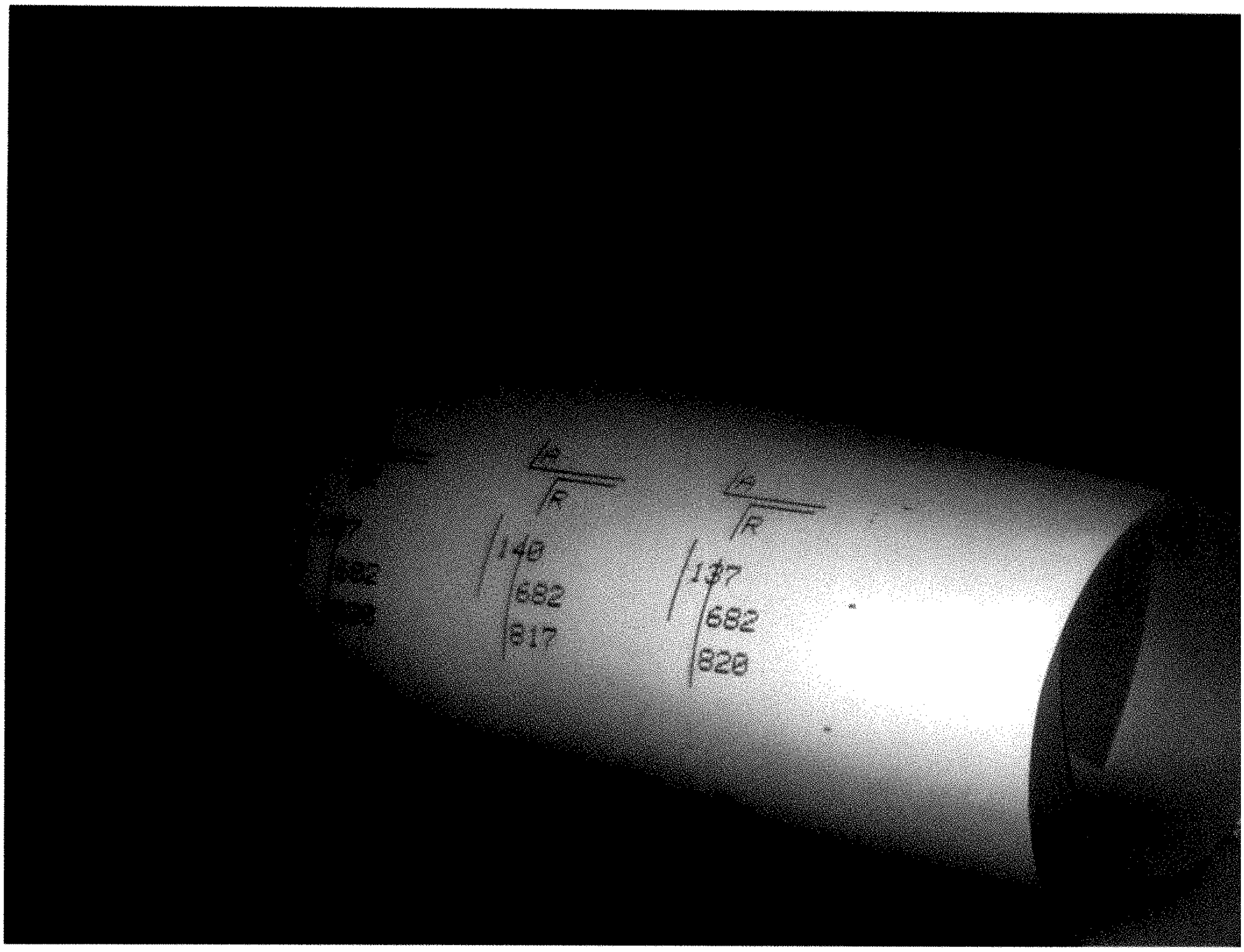

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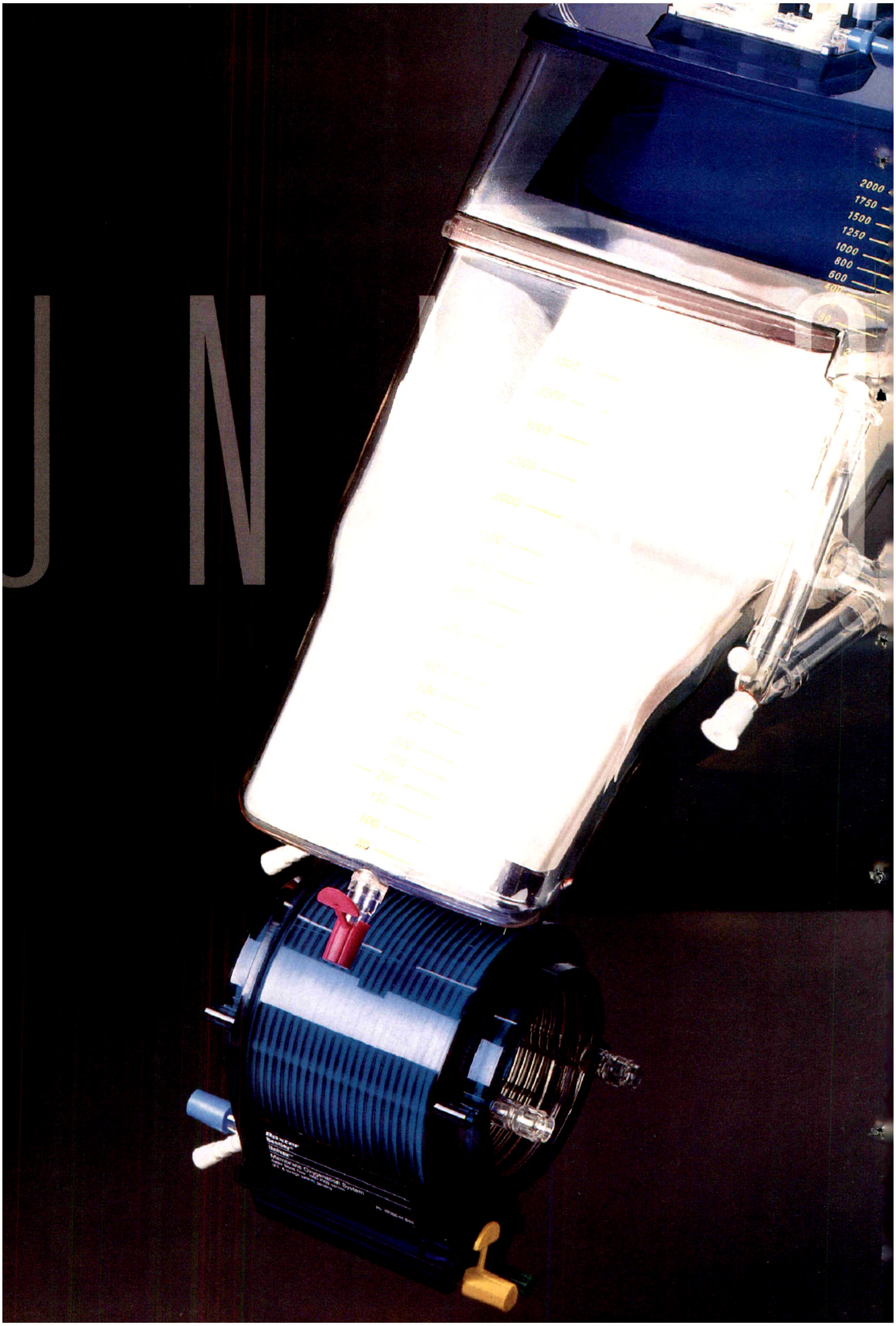
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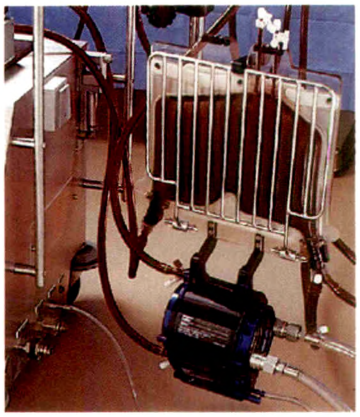

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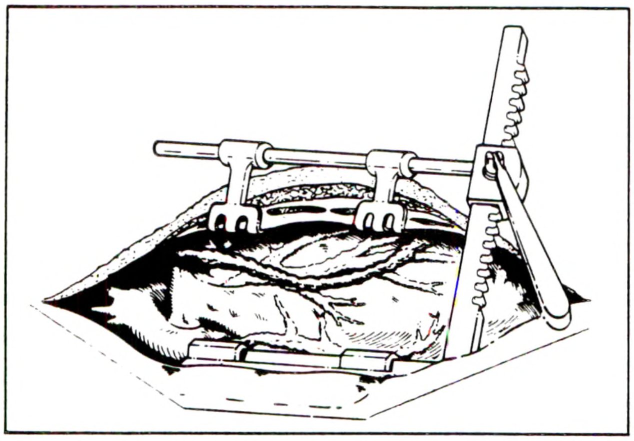

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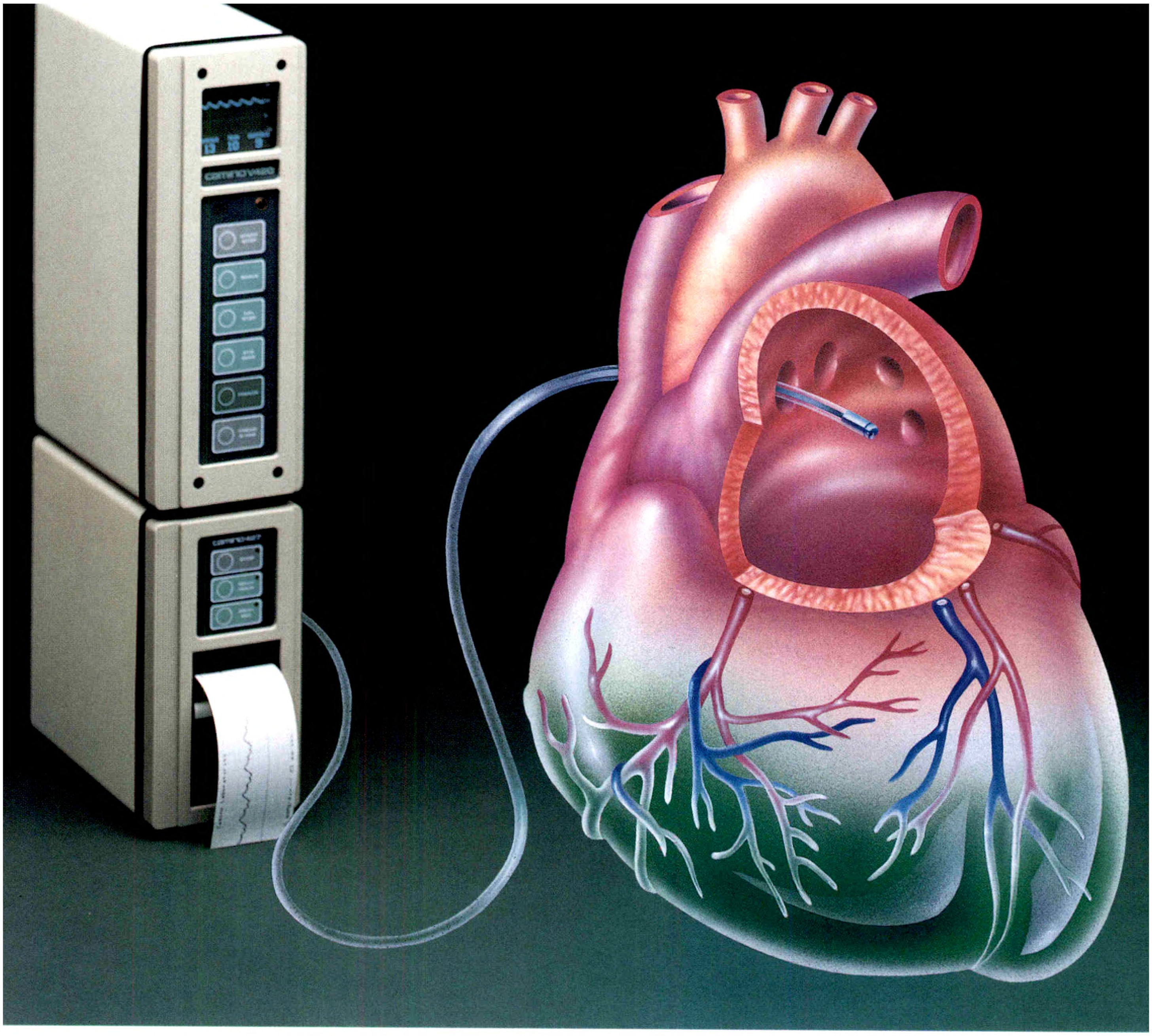

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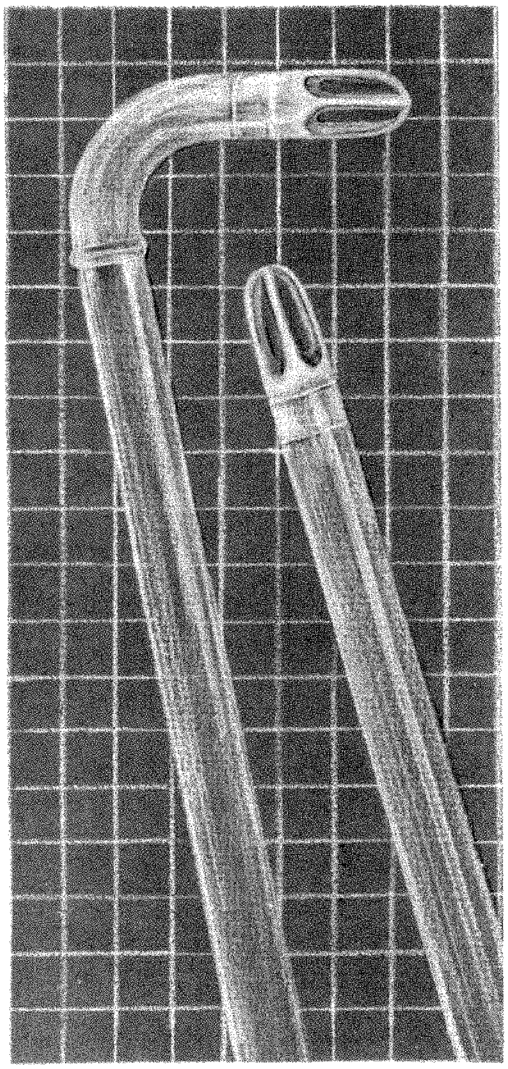

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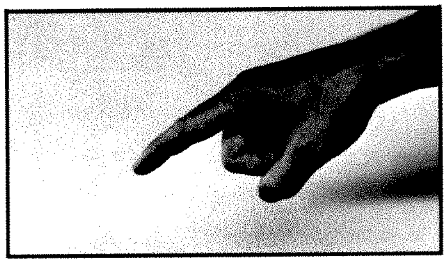

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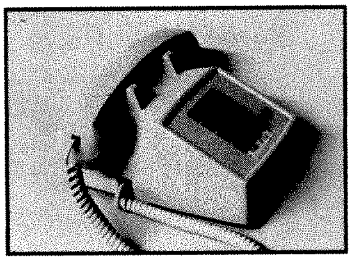

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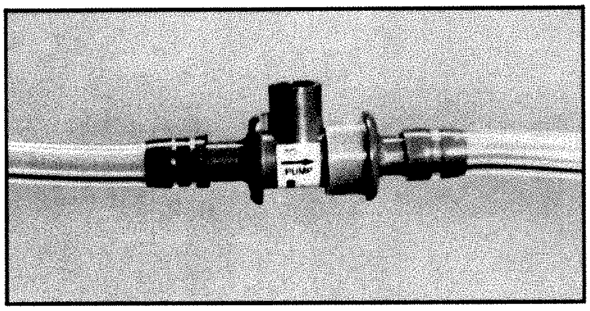

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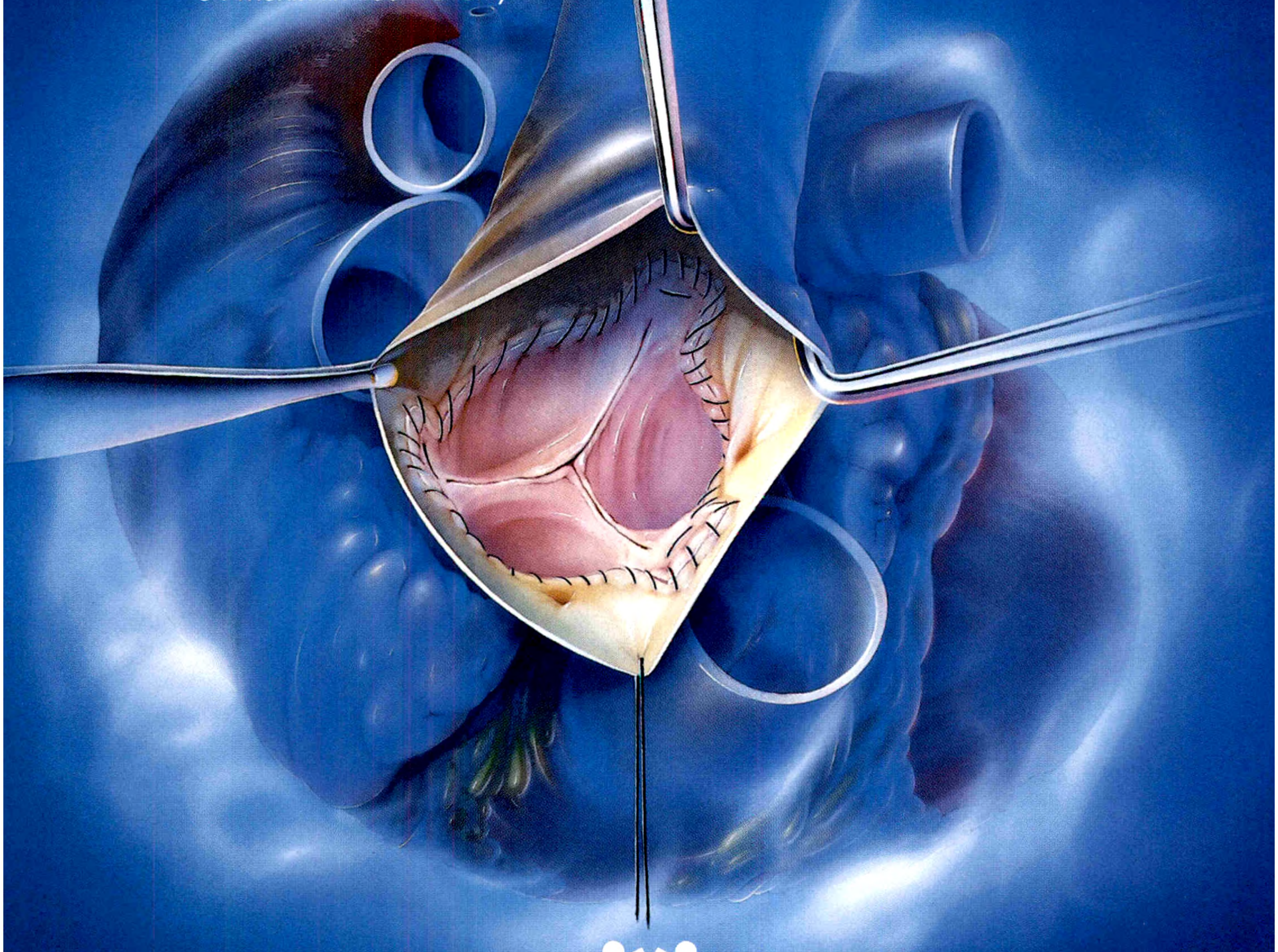

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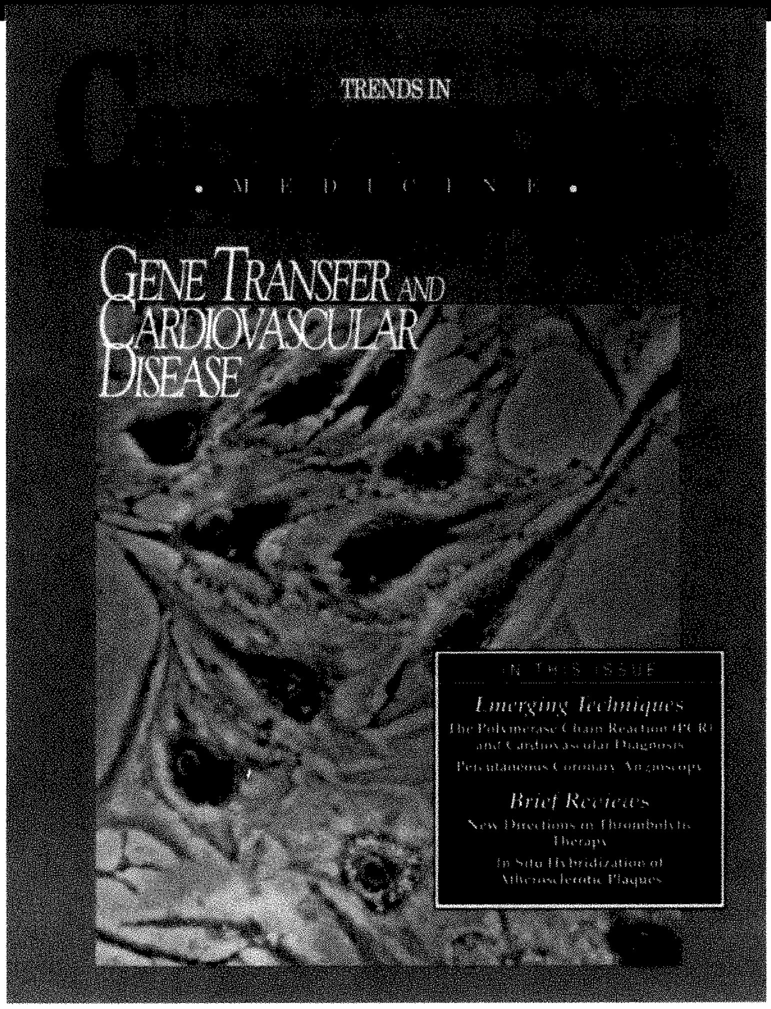
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Empyema Thoracis

Joseph I. Miller, MD

Division of Cardio-Thoracic Surgery, Joseph B. Whitehead Department of Surgery, Emory University School of Medicine, Atlanta, Georgia

The practice of thoracic surgery began with the drainage of pus from the chest by Hippocrates, who wrote extensively on this subject, describing symptoms and natural history [1]. The history of the management of empyema and the evolution of its surgical treatment is a major aspect of the development of thoracic surgery. Current modalities used in the treatment of thoracic empyema include thoracentesis, intercostal tube drainage, rib resection with tube drainage, open rib drainage, decortication, excision with exenteration (or empyemaectomy), sterilization of thoracic cavity, thoracoplasty, and muscle flap closure. Each of these modalities has a role and an appropriate time and place in the treatment of acute and chronic thoracic empyema.

The article in this issue by Ali and Unruh [2] presents an extensive experience with 65 adult patients treated. Their etiologic distribution parallels that of other series in the literature [3]. More than 50% of thoracic empyemas are directly related to pyogenic pneumonia. Approximately 25% occur as sequelae after operation in the thorax on the esophagus, lungs, or mediastinum. The third most common cause is extension of a subphrenic abscess, occurring in 8% to 11%. Other causes are secondary to rupture of a lung abscess, generalized pulmonary sepsis, and miscellaneous causes. *Staphylococcus aureus* is the most common etiologic organism in both pediatric and adult empyema. It is cultured in approximately 92% of the pediatric age group and in more than 50% of adult patients. The gram-negative organisms, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Aerobacter aerogenes*, *Proteus*, and *Salmonella* are very common in the adult population. The majority of adult patients have more than one organism cultured from the pleural fluid, with an average of 2.3 organisms per patient.

See also page 355.

In the group of patients reported by Ali and Unruh, there was a total of 34 (52%) who were seen with postpneumonic empyema. Ali and Unruh stated that all but one of these required rib resection under local or general anesthesia. In contrast, we have used closed chest tube thoracotomy as the predominant means of managing simple empyema. From 1974 to 1990, we have managed more than 90 cases of postpneumonic thoracic empyema by simple chest tube thoracostomy with closed drainage and ultimate conversion to an empyema tube with slow advancement out over a period of 6 to 8 weeks. There were only 4 cases in which this was not successful when the thoracic space had been well-drained by closed chest tube thoracostomy. Only 2 cases required an open procedure in this group of patients.

At the same time, we have operated on 52 patients who had a multiloculated parapneumonic empyema that had not been adequately drained by closed chest tube thoracostomy. In this group, the empyema had been present from 3 to 12 weeks. All of these patients underwent open thoracotomy with decortication and drainage, and there were only 2 patients requiring muscle transposition to fill a residual space. Ali and Unruh noted that 12 patients (30%) in the group who had previous rib resection required open thoracotomy, and 9 patients required muscle transposition. This has not been our experience in patients who had decortication within 3 months of the onset of the empyema. Intrathoracic muscle transposition has rarely been required in the management of postpneumonic empyema. Perhaps the increased use of intrathoracic muscle flap transposition by Ali and Unruh may have been because the operation was performed at a later time than the inception of the empyema. In our experience, in the usual case of multiloculated parapneumonic empyema in which open thoracotomy and decortication are required, muscle flap transposition is rarely necessary. Our institution tends to proceed with early surgical intervention at 3 to 4 weeks when standard chest tube thoracostomy does not relieve the majority of the loculated fluid, as the surgical risk is less than 1%, and the expected outlook is good in more than 95% of patients. There is a short hospitalization of 8 to 10 days, and all tubes are removed at the time of discharge. I have operated on 52 patients with a multiloculated parapneumonic empyema with no operative mortality and good results in 50 of 52 patients. Prolonged chest tube sinuses and drainage, which required second operations to close, ultimately developed in 2 patients.

Ali and Unruh present 16 patients with postresectional empyema, 9 acute and 7 chronic. There were 3 patients who had a pneumonectomy and 6 who had a lobectomy as the initial procedure. Ali and Unruh have correctly stated that treatment must be varied for each case and individually tailored for each patient. Our institution rarely uses thoracoplasty in the management of a postresectional empyema space, and we believe that the majority of postresectional spaces can be filled by intrathoracic muscle transposition of the appropriate muscle flaps. Flaps used in the order of frequency are (1) latissimus dorsi; (2) serratus anterior; (3) pectoralis major; (4) omentum, and (5) rectus abdominis. The omentum is particularly useful in closing lobar or main bronchopleural

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fistulas [4, 5]. A thoracoplasty is rarely required in the postlobectomy resectional empyema space in which intrathoracic muscle flaps have been transposed. An upper lobectomy space can be easily filled with a pectoralis major flap placed through the second intercostal space. A lower lobectomy space can be filled with latissimus or rectus abdominis. In the postpneumonectomy space, occasionally two to three ribs may need to be resected to obliterate any remaining major space after intrathoracic muscle transposition. We have treated 17 patients with postpneumonectomy empyema by single-stage complete muscle flap closure of the empyema space, with greater than 75% experiencing excellent results [5]. In addition, we have used intrathoracic muscle flap transposition in the treatment of five lobectomy empyema spaces with good results in all cases.

Ali and Unruh have correctly pointed out that posttraumatic empyema and/or hemothorax should be treated early with decortication and appropriate evacuation and drainage. In all of these patients, the lung immediately reexpands, and the long-term outlook is excellent. Early decortication and drainage should be considered in the case of a clotted hemothorax in which the clot is not removed within 5 to 7 days of chest tube thoracostomy. Occasionally, streptokinase can be injected into the clotted hemothorax space with fairly good results, but, more than likely, early decortication and evacuation of the clot will be required.

In conclusion, Ali and Unruh have presented an interesting and detailed analysis of a complex group of patients. Their management and long-term results are excellent. We would tend to favor closed chest tube thoracostomy rather than rib resection in the management of the majority of cases of simple postpneumonic empyema. In those patients with multiloculated empyema that does not respond to closed chest tube thoracostomy, early decortication and drainage is successful in greater than 95% of all cases. Morbidity is lessened, and long-term outlook is excellent. In the remainder of their three groups, our mode of management would be same.

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Aspirin, Blood Loss, and Transfusion

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Although aspirin is the most commonly used and widely studied, it is certainly not the only drug available that alters the coagulation mechanism that is currently being given to patients with cardiovascular diseases. Stein and associates [1] have recently published an exhaustive review of the role of antiplatelet agents in cardiovascular disease. In summary, aspirin in low to moderate doses (75 to 325 mg daily) has proved beneficial in (1) preventing the secondary events in patients with symptomatic cerebral vascular disease, (2) preventing acute vessel occlusion during coronary angioplasty (but it has been ineffective in the prevention of restenosis), (3) decreasing the mortality of acute myocardial infarction and reducing the subsequent reinfarction rate, and (4) reducing the mortality and infarction rates in patients with unstable angina. Because of these beneficial effects of aspirin in patients with cardiovascular disease, many, if not most, patients now coming to coronary revascularization are taking aspirin. The report by Taggart and associates [2] that appears in this issue of *The Annals* concerning operative and postoperative blood loss in patients taking aspirin is particularly timely. Although they found that aspirin administration was associated with increased perioperative blood loss and transfusion requirements, the overall hospital stay was not prolonged.

See also page 425.

Aspirin, by its acetylation of cyclooxygenase, inhibits the formation of thromboxane A_2, a strong stimulus to platelet aggregation and vasoconstrictor. This effect on platelet cyclooxygenase is permanent, persisting for the life of the platelet—as the platelet does not have the capacity to synthesize cyclooxygenase de novo. Therefore, in order for the patient to have a population of completely functional platelets at the time of operation, aspirin administration must be stopped a week or more preoperatively or the patient must be given transfusions of platelet concentrates. Vascular endothelial cells, unlike platelets, do have the capacity to synthesize cyclooxygenase and therefore rapidly regain their ability to produce the vasodilator prostacyclin within a few hours after cessation of aspirin therapy. Prostacyclin, like thromboxane A_2, is a product of arachidonic acid metabolism; its formation is initiated by cyclooxygenase [3, 4].

Perioperative blood loss and the requirement for transfusion has become a major concern in patients undergoing cardiac operations. The use of anticoagulants such as warfarin in patients with valve prostheses or dilated hearts with arrythmias; the use of aspirin, dipyridamole, nonsteroidal antiinflammatory agents, and other platelet inhibitors in patients with coronary disease; and the administration of tissue plasminogen activator, thrombolytic enzymes, and heparin in the acute coronary occlusion setting have all brought this problem into very clear focus. The prevalence of transfusion-transmitted diseases has only served to amplify the concern. Similarly, the increasing number of reoperations has been attended by increased transfusion requirements. The present practice by blood banks of "cannibalizing" whole blood in order to make the most of all of its components has left us with the necessity of using red blood cell concentrates and crystalloid to restore blood volume in most instances.

The report by Taggart and associates appropriately calls our attention to this issue and concludes with the recommendation that, when possible, aspirin be discontinued 1 week or more before an elective operation. I agree with this recommendation, but would like to go even farther. Our blood banks should be encouraged to provide fresh (less than 48 hours old) whole blood for use in cardiac operations, particularly in patients who have recently received aspirin or other antiplatelet agents. Additionally, there is promising new information that the use of aprotinin (Trasylol) during cardiopulmonary bypass may offer some protection from the mechanical damage to platelets during open heart operations [5]. Observations like those of Taggart and associates are important and more reports of this type are needed to substantiate the magnitude of this problem.

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The Medtronic-Hall Valve: Frequently Used, Seldom Reported

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After the pioneering work of Hufnagel, Starr, and Harken using caged-ball valves, it became apparent that a valve with a more central blood flow and a lower profile would be advantageous. Dr Juro Wada [1] designed a hinged pivoting-disc valve, demonstrating that a lower profile and central flow design were possible. Encouraged by this work, the Björk-Shiley valve and the Lillehei-Kaster valve were developed almost simultaneously. Although both of these hingeless pivoting-disc valves were an improvement over the Wada valve, they were still limited by the opening angle of the poppet. In addition, the relatively small minor orifice was responsible for occasional thrombus formation [2, 3]. The Björk-Shiley valve was modified to the familiar convexoconcave disc model. Mr Robert Kaster, who engineered the Lillehei-Kaster valve, collaborated with Karl Victor Hall and designed the Medtronic-Hall valve, with a much larger minor orifice and a disc opening angle of 75 degrees in the aortic and 70 degrees in the mitral valve models. The excellent hemodynamic performance of the Medtronic-Hall valve has been known for some time [4], and its durability has made it the valve of choice in artificial heart designs [5, 6]. This valve's popularity has increased considerably since the Björk-Shiley valve was removed from the market, but there is still a relative paucity of long-term clinical reports regarding its effectiveness.

See also page 429.

Vallejo and associates [7] report in this issue an 8-year clinical experience with 444 Medtronic-Hall heart valve prostheses implanted in 351 patients at the General Hospital Gregorio Marañon between January 1981 and September 1986. Various other prostheses were in use in the institution during that period. The practice of Vallejo and associates was to implant porcine bioprostheses in patients more than 70 years old and in patients in whom anticoagulation was contraindicated. In the remaining patients, mechanical prostheses were used. The choice of which mechanical prosthesis to use was left up to the individual surgeon's preference. This is consistent with the practice at many cardiothoracic surgical centers. Certainly groups of surgeons who routinely implant only bioprostheses or only mechanical prostheses are a small minority.

Mortality

The overall hospital mortality was 6.2%, whereas there was a 25% to 50% mortality in patients in whom the tricuspid valve was replaced. The cross-section of the right ventricle at the level of the tricuspid valve is more oval than round. Implantation of a pivoting-disc valve may lead to the excursion of the disc being impeded by the right ventricular muscle, causing valve thrombosis [8]. Certainly porcine xenografts or other tissue valves seem to offer a safer alternative when replacement of the tricuspid valve is necessary [9].

Thromboembolism

The thromboembolic rates observed by Vallejo and associates are fairly low and are similar to the incidence reported by others [10]. Reports from a third world country on a large series of patients with implanted Medtronic-Hall valves support the findings of a low embolization rate, even in a less privileged population [11]. Another report from the United Kingdom demonstrated a low embolic rate using this valve despite a fairly low level of anticoagulation with Coumadin, thus decreasing the incidence of bleeding complications [12].

Endocarditis

Vallejo and associates report an overall incidence of prosthetic valve endocarditis of 5.4%, of which 47% occurred in the early postoperative period. This figure is somewhat higher than those generally seen in valve replacement series and raises the question of the perioperative antibiotic coverage used. Certainly past reports have shown that, without antibiotic coverage, the incidence of prosthetic valve endocarditis can be as high as 10% [13]. In a large review of various valve replacement series covered adequately with antibiotics, the overall incidence tended to be closer to 2% [14].

Hemolysis

Vallejo and associates report 8 patients in whom hemolysis was present. The severity of this complication is not detailed, and it was believed that, at least in 2 patients, the cause was not mechanical. In the remaining 6 patients, the blame was placed on either a periprosthetic leak or an intrinsic valvar cause. Our own experience indicates that the serum lactate dehydrogenase values were slightly above the normal range in patients who had undergone valve replacement with the Medtronic-Hall

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valves [15]. Only 2 of more than 450 patients had clinically significant elevations in lactate dehydrogenase; both of these patients were reoperated on for noninfectious perivalvar leak. At the time of operation the leaks were repaired, with the result that the lactate dehydrogenase values promptly fell to the slightly-above-average values (Starek PJK, unpublished data). Hemolysis due to even small perivalvar leaks has been well documented [16], and it is quite probable that patients with clinically significant hemolysis have either a perivalvar leak or some intrinsic increase in red cell fragility.

Valve Impingement

Interference with disc motion by sutures, chordae, or cardiac muscle has sometimes been referred to as disc impingement, particularly when the disc becomes fixed in one position. This condition is a potential hazard in all disc valves, but is almost entirely preventable or correctable by the surgeon familiar with the implantation of pivoting-disc valves [17]. Vallejo and associates detected four such problems intraoperatively and corrected the situation without difficulty.

Conclusions

Vallejo and associates conclude that the Medtronic-Hall valve has proved to be a reliable prosthesis without structural failures, with fine hemodynamic performance, and with low thromboembolic rates. Their long-term data justify these conclusions. Our personal experience with this valve over a 12-year period in more than 450 patients is very similar and would also support these conclusions.

No currently available prosthetic valve is suitable for all patients requiring valve replacement. Some patients clearly require the use of tissue valves, whereas the pivoting-disc valves continue to offer excellent hemodynamics, good laminar flow, and, in the case of the Medtronic-Hall valve, superior durability.

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Cardioplegia for Transplantation: Failure of Extracellular Solution Compared With Stanford or UW Solution

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Crystalloid cardioplegia with an extracellular fluid formulation is widely used for donor heart protection. A survey of 109 transplant programs yielded 62 replies with 42% of respondents using variations of extracellular solution and 45% using the dextrose and mannitol–based Stanford solution. These two commonly used clinical solutions and University of Wisconsin (UW) solution, which has had success in clinical hepatic and renal transplantation, were compared in a canine model of cardiac transplantation. After antegrade hypothermic cardioplegic arrest, the experimental hearts were excised and stored at 4°C for 6 hours (n = 29). An oxygenated, blood-primed isolated heart preparation was used for reperfusion. After a rest of 45 minutes, cardiac output was increased against constant afterload until a left atrial pressure of 15 mm Hg was reached. The maximum cardiac performance measured by cardiac index, minute work, and stroke work was highly significantly better with Stanford or UW solution protection than with the extracellular solutions ($p < 0.0001$). Assuming a cardiac index of 50 mL · kg^{-1} · min^{-1} is necessary for successful separation from cardiopulmonary bypass, only 1 of 14 extracellular and 15 of 15 Stanford and UW animals would have survived ($p < 0.0001$). This study strongly suggests that extracellular cardioplegia is inferior for cardiac transplantation and that programs using this solution should reevaluate their method of myocardial protection for donor hearts.

(Ann Thorac Surg 1990;50:348–54)

Cardiac transplantation is an accepted treatment for end-stage cardiac failure in select patients, and the resultant demand for donor hearts grows yearly. Most hearts are now obtained through distant procurement, which has improved access to the finite donor pool [1]. This increases the period of donor organ myocardial ischemia, which is known to affect early homograft function and patient survival [1].

One aspect of donor myocardial protection under the control of the surgeon is the donor cardioplegia technique. A model of donor heart procurement with prolonged ischemic time and transplantation was developed. The most commonly used variations of clinical donor cardioplegic solutions and an experimental solution were evaluated to determine the effect of different protection schemes on donor heart function.

A survey of the active cardiac transplant programs in the United States was made to determine current donor cardioplegia practices. With the assistance of the Registry of the International Society for Heart Transplantation, an evaluation of early patient outcome based on donor cardioplegia technique was made.

Material and Methods

Laboratory Study

Twenty-nine dogs seronegative for *Dirofilaria* and ranging in mass from 25 to 36 kg were studied. The animals were preanesthetized with intramuscular administration of morphine sulfate, 4 mg/kg, and anesthetized with intravenous administration of sodium pentobarbital, 30 mg/kg. They were intubated orotracheally and placed on a volume-cycled ventilator. A median sternotomy incision was made, and an arterial monitoring line was placed at the intrathoracic left subclavian artery. The great vessels were dissected and prepared for subsequent ligature or tourniquet control. Mobilization for an extrapericardial excision of the heart was completed. The pericardium was included with the donor heart to facilitate subsequent suspension of the heart in the isolated, perfused, working mode.

After arterial blood gas confirmation of satisfactory oxygenation, ventilation, and acid-base balance, the animals were given heparin sodium, 3 mg/kg, intravenously. Excision of the heart was begun after inflow occlusion and then antegrade aortic root infusion of one of the four cold cardioplegic solutions (Table 1) at a constant pressure of 50 mm Hg. Prompt diastolic arrest occurred uniformly. The heart was vented by transection of the inferior vena cava and incision of the left atrial appendage. Myocardial cooling was supplemented by topical cold balanced saline solution. The total cardioplegia dose delivered approxi-

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Table 1. Comparison of Cardioplegic Solutions[a]

Component	Extracellular Composition Fluid 1	Extracellular Composition Fluid 2	Stanford University Composition Fluid	Component	University of Wisconsin Solution
Na^+	185	155	20	KH_2PO_4	25 mmol
K^+	24	24	27	$MgSO_4$	5 mmol
Mg^{2+}	2.9	2.9		Adenosine	5 mmol
Cl^-	95	95	27	Glutathione	3 mmol
Acetate$^-$	26	26		Raffinose	30 mmol
HCO_3^-	49	19	20	Allopurinol	1 mmol
Gluconate	22	22		Potassium lactobionate	100 mmol
Glucose	0.15%	0.15%	4.5%	Pentastarch	5%
Mannitol	. . .	. . .	1.14%	Heparin	1,000 IU/L

[a] All data are shown in milliequivalents unless otherwise stated.

Cl^- = chloride ion; HCO_3^- = bicarbonate radical; K^+ = potassium ion; KH_2PO_4 = potassium phosphate; Mg^{2+} = magnesium ion; $MgSO_4$ = magnesium sulfate; Na^+ = sodium ion.

mated the clinical use of about 3 mL/g of heart (with the assumption that the average canine heart mass to total body mass ratio is approximately 9 g/kg).

The heart, proximal great veins, main pulmonary artery, and aorta past the left subclavian artery were excised and stored at 3° to 4°C in a solution with the same composition as the cardioplegia chosen for that heart. Near the end of the ischemic period, the left atrium and aorta were cannulated through the innominate artery in preparation for reperfusion. The left atrial and aortic pressures were monitored with strain-gauge manometers.

A cardiopulmonary bypass circuit was primed with homologous blood and crystalloid to a hematocrit of 0.20. The pH was adjusted to 7.4 with sodium bicarbonate as needed. Lidocaine hydrochloride was added to a calculated therapeutic level of 3 μg/mL. Air was displaced from the heart, and the heart was connected to the cardiopulmonary bypass circuit (Fig 1). The tricuspid valve was excised, and the main pulmonary artery and superior vena cava were ligated, directing all thebesian and coronary sinus flow to the inferior vena cava. The caval flow was then collected by gravity and directed to the venous reservoir.

At 6 hours, the heart was removed from the 4°C bath and underwent controlled reperfusion with normothermic oxygenated blood at 50 mm Hg for 5 minutes. Mean aortic pressure was then increased to 80 mm Hg and kept there for the remainder of the experiment (Fig 2). The heart was electrically defibrillated as needed at 5 minutes and subsequently at 10, 20, and 30 minutes if persistent ventricular fibrillation was present. At 30 minutes, a bolus of 10 μg of isoproterenol was given and a constant infusion of 0.25 μg/min was begun.

At 45 minutes after reperfusion, the heart was switched to the working mode (Fig 3). The heart was made to pump against a mean arterial pressure of 80 mm Hg by the infusion of oxygenated blood into the left atrium. An infusion flow of 500 mL/min was increased by 250 mL/min until the left atrial pressure reached 15 mm Hg. The maximum cardiac output for each heart was determined to be the maximum cardiac output obtained with the mean arterial pressure at 80 mm Hg and the left atrial pressure at less than or equal to 15 mm Hg. If the heart was unable to pump 500 mL initially with a left atrial pressure less than or equal to 15 mm Hg, the cardiac output was considered to be 0.

Hemodynamic data were gathered through an analog to digital conversion board (Data Translation, Inc) and stored and analyzed through a 386 microprocessor using an interactive program developed in this laboratory (James A. Bradford, PhD).

Hemodynamic calculations were based on these formulas:

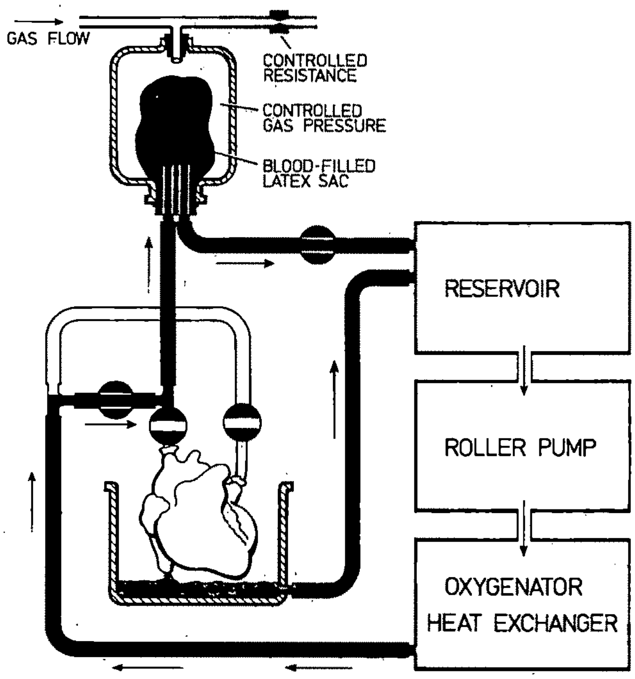

Fig 1. The working heart model after priming of the circuit.

Stroke work = cardiac output (mean aortic pressure − mean left atrial pressure) · 0.0136/heart rate

Minute work = cardiac output (mean aortic pressure − left atrial pressure) · 0.0136

All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Clinical Correlation

A survey of cardiac transplant programs active in the United States was made. This mailing was based on the list of participants in the United Network for Organ Sharing. The program directors were asked to describe their current cardioplegia technique for donor heart procurement. A choice was given between the four categories shown in Appendix 1 or, alternatively, the cardioplegic solution components and physical characteristics could be listed on a detailed checklist provided in the mailing.

The cardioplegia techniques of the respondents were categorized into extracellular variations, Stanford solution, or other techniques. The programs were then listed by technique and submitted to Dr Michael Kaye at the Registry of the International Society for Heart Transplantation. The number of transplant patients in the registry accounted for by these programs and the 30-day mortality rates were determined. This information was returned grouped by the specific cardioplegia category and without individual program identification, which preserved the confidentiality of the international registry participants.

Statistical Analyses

Statistical analyses were carried out on a microprocessor using proprietary software with the advice of a statistician (Compaq 386/20e; RS1 release 4.0, BBN Software Products Corporation; Elmer Hall, PhD, Emory University). The comparison of the difference in overall mortality between the Stanford and extracellular groups in the clinical survey was made by χ^2 analysis or Fisher's exact test with a significant difference said to exist at a p level of less than 0.05. Evaluation of the hemodynamic data between the four cardioplegia groups was made first with the Kruskal-Wallis statistic. When a significant difference was noted, the groups were compared using individual nonpaired t tests with a significant difference said to exist at a p level of less than 0.05. Fisher's exact test was used to compare projected mortality between the Stanford plus University of Wisconsin (UW) experimental groups and the extracellular 1 plus extracellular 2 experimental groups. A significant difference was said to exist at a p level of less than 0.05.

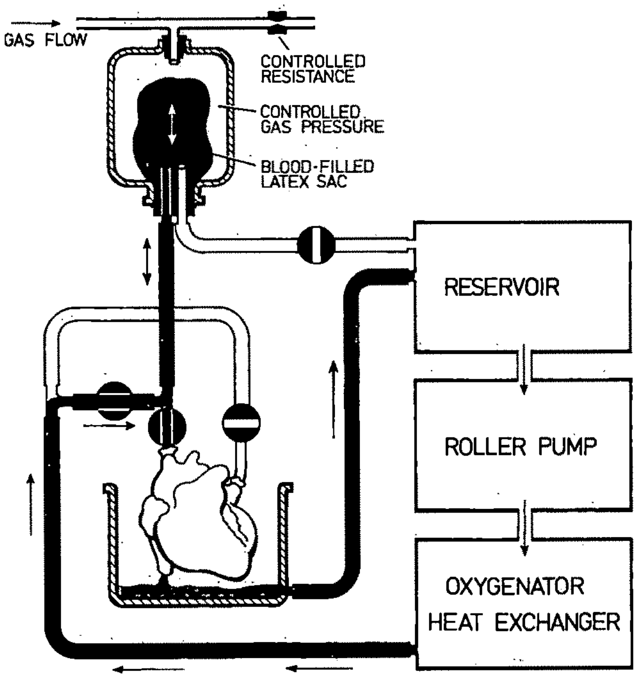

Fig 2. Controlled cardiac reperfusion with oxygenated blood into the aorta for 45 minutes.

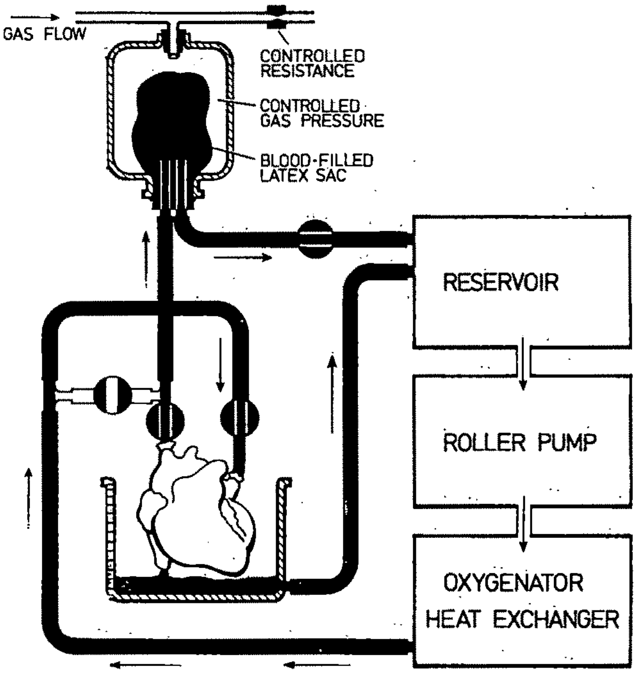

Fig 3. Roller-pump–controlled oxygenated blood flow to the left atrium to yield the working heart.

Results

Laboratory Study

On reperfusion, the hearts protected by extracellular type 1 or 2 solution all exhibited marked swelling, and the majority were not able to sustain an organized rhythm or perform work against the aortic pressure. In stark contrast, the hearts protected by Stanford or UW solution appeared less edematous and had fewer rhythm disturbances, and all had cardiac outputs compatible with survival of the "recipient."

The hemodynamic results of the myocardial protection afforded by the four different solutions are summarized in Figures 4 through 8 and Table 2. Statistical comparison between groups is provided in Table 2.

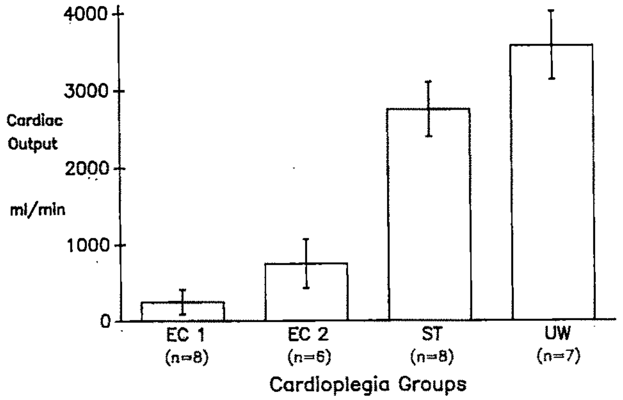

Fig 4. Maximum mean cardiac output at a left atrial pressure of 15 mm Hg (p < 0.0001 by Kruskal-Wallis statistic). (EC = extracellular cardioplegia; ST = Stanford solution; UW = University of Wisconsin solution.)

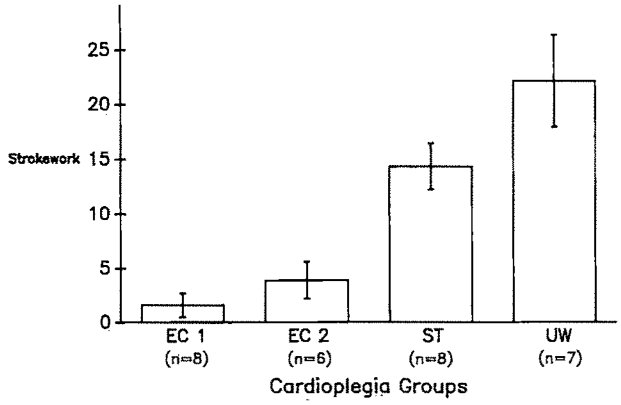

Fig 6. Maximum mean stroke work at a left atrial pressure of 15 mm Hg (p < 0.0001 by Kruskal-Wallis statistic). Abbreviations are the same as in Figure 4.

Clinical Correlation

There were 62 respondents to the mailing of the donor heart cardioplegia survey. This is within the framework of a reported 109 active centers in the United States as of 1987 [1]. Forty-five percent of the programs used the dextrose and mannitol–based Stanford solution. An extracellular composition was used by 42%. The others responding reported a variety of other techniques and will not be considered further here.

A total of 1,423 patients received either an extracellular- or Stanford-protected heart. The overall mortality between these two groups was not significantly different. Sixty-six (10%) of 660 patients with extracellular cardioplegia–protected hearts died within 30 days of transplantation as did 70 (9.2%) of 763 patients receiving Stanford solution–protected hearts. The effect of ischemic time on outcome based on 30-day mortality is demonstrated in Figure 9. Eighty percent of the respondents using a variation of the extracellular fluid indicated that was also the method for their standard cardiac procedures. Fifty-six percent of the respondents using Stanford solution employed that solution for standard cardiac procedures.

Comment

More than 1,400 cardiac transplantations were done in the United States in 1987. Although the number of transplantations per year continues to grow, catalyzed by increasingly successful immunosuppression, there remains a large gap between donor availability and recipient need. In response to this problem, efforts have broadened the geographical base for organ donation in such a way that almost 60% of transplanted hearts are procured at distant sites [1]. Distant procurement was demonstrated by the Stanford [2, 3] and Richmond [4] groups to be effective and led to an increase in the number of cardiac transplantations performed. As the distance for organ procurement increases, the myocardial ischemic period and the risk of early cardiac dysfunction and mortality increase [1]. This effect appears to be minimal if ischemic times are less than 4 hours [5]. Also as the duration of ischemia increases, the

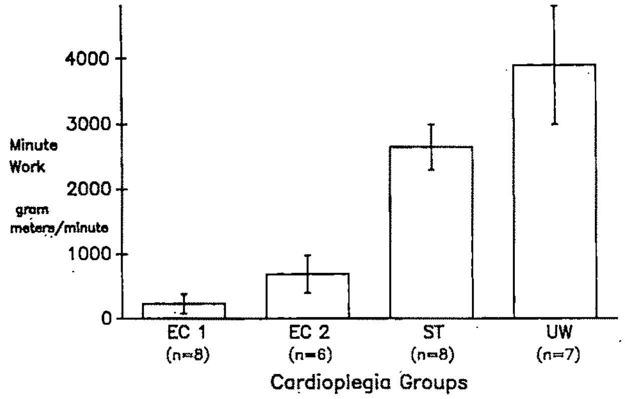

Fig 5. Maximum mean minute work at a left atrial pressure of 15 mm Hg (p < 0.0001 by Kruskal-Wallis statistic). Abbreviations are the same as in Figure 4.

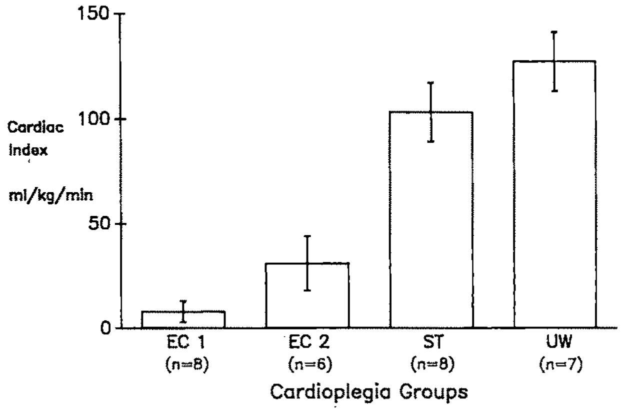

Fig 7. Maximum mean cardiac output indexed to donor dog body mass at a left atrial pressure of 15 mm Hg (p < 0.0001 by Kruskal-Wallis statistic). Abbreviations are the same as in Figure 4.

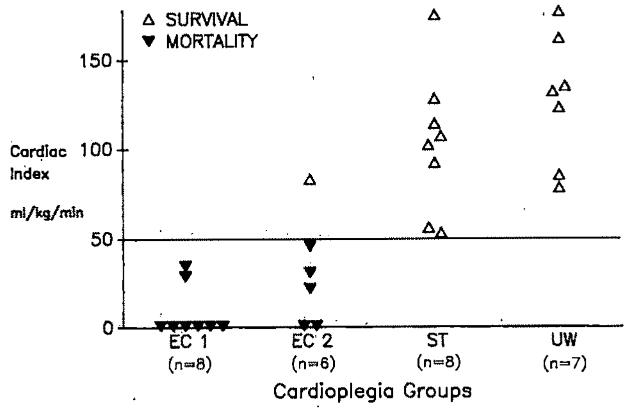

Fig 8. Survival by ability to achieve a cardiac index of 50 mL · kg^{-1} · min^{-1}. Abbreviations are the same as in Figure 4.

impact of the myocardial protection technique on ultimate cardiac function is more profound. Despite laboratory and clinical successes with the use of hypothermic perfusion for donor protection, hypothermic cardioplegic protection remains the clinical gold standard [6, 7].

Fundamental to myocardial protection for transplantation is rapid establishment and maintenance of hypothermia, which was documented early on by Lower and co-workers [8]. The supplemental beneficial effects of cardioplegia are documented [3, 9–11]. This is an area under a high degree of control by the surgeon. This study, therefore, was designed to study effects of current clinical and experimental methods of cardioplegic protection of the donor heart to determine if differences exist that might be exploited to improve early donor heart function.

The actual practice of donor heart cardioplegic protection was examined with a survey of active programs. There was a substantial response, which translated into data on more than 1,400 cardiac transplant patients. Eighty-seven percent of the responding programs were placed into one of two fairly homogeneous groups with respect to donor cardioplegia technique. About equal numbers used the Stanford cardioplegic solution or a variation of an extracellular solution. The widespread use of the Stanford solution is probably a reflection of the pioneering efforts of that group in developing the operation, achieving ongoing excellent clinical results, and training many of the directors of currently active cardiac transplant programs. The similarly extensive use of an extracellular composition cardioplegic solution may reflect the extension of the technique used for standard cardiac procedures at a particular institution. Eighty percent of extracellular solution users also employed that method for cardiac protection during standard operations.

For the laboratory investigation, four cardioplegic solutions were evaluated. The Stanford composition was as published and confirmed by the Stanford Hospital Pharmacy [2]. Two extracellular compositions were included. Extracellular 1 is that used previously for canine cardioplegia in this laboratory. Extracellular 2 is the clinical standard for cardiac operations at Emory University Affiliated Hospitals, which is similar to extracellular solutions in widespread clinical use as confirmed by the survey.

Table 2. Hemodynamic Outcome for Different Cardioplegia Groups: Laboratory Study[a]

Group	Maximum Cardiac Output (mL/min)	Maximum Minute Work (g-m/min)	Maximum Stroke Work (g-m)
EC1	250 ± 160	230 ± 150	1.6 ± 1.1
EC2	750 ± 320	686 ± 290	3.9 ± 1.2
ST	2,750 ± 350	2,640 ± 350	14.3 ± 2.1
UW	3,570 ± 440	3,890 ± 900	22.1 ± 4.2

[a] Significance: EC1 versus EC2, not significant; EC1 versus ST, $p < 0.05$; EC1 versus UW, $p < 0.05$; EC2 versus ST, $p < 0.05$; EC2 versus UW, $p < 0.05$; and ST versus UW, not significant.

EC1 = extracellular cardioplegia, laboratory; EC2 = extracellular cardioplegia, clinical; ST = Stanford cardioplegic solution; UW = University of Wisconsin solution.

The UW solution has shown promise in clinical preservation of solid organs for transplantation [12, 13] and has shown benefit in laboratory studies for myocardial protection [14]. It was included as a fourth solution tested in this model.

These solutions were studied in a model designed to simulate the clinical procurement, extended storage, and initial function of the implanted heart. The procurement and storage phases are nearly identical with those in current clinical practice. Chronotropic and inotropic support was uniform across all groups in the form of isoproterenol, which is in line with clinical transplant practice [15]. To minimize experiment to experiment variability inherent in use of different recipient animals, we employed this isolated heart model in which hematocrit, acid-base balance, aortic pressure, cardiac output, and temperature were controlled. Respiratory and hormonal variability and autonomic effects on the peripheral circulation, all known to affect cardiac function, were eliminated.

The results demonstrate a clear advantage of the dextrose and mannitol–based Stanford solution and the UW solution over both of the extracellular solutions for early cardiac function after 6 hours of hypothermic ischemic

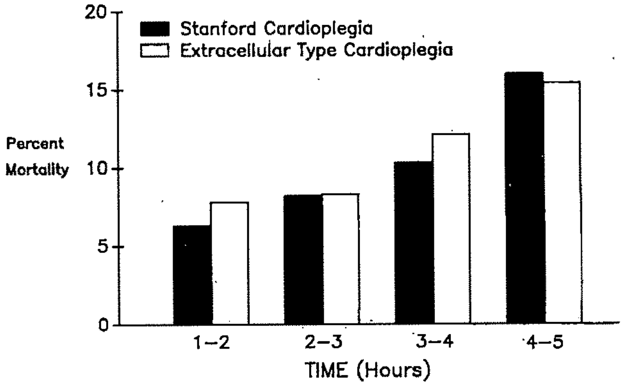

Fig 9. Thirty-day mortality of transplant patients from the clinical survey by time of ischemia and by cardioplegia group.

protection. No significant difference existed between the Stanford and UW groups or between the two extracellular groups.

Assuming that a criterion for successful separation from cardiopulmonary bypass is a cardiac index of 50 mL · kg^{-1} · min^{-1}, all 15 UW and Stanford hearts would be "survivors," but only 1 of the 14 extracellular 1 and extracellular 2 hearts could achieve an index greater than 50 mL · kg^{-1} · min^{-1}.

Principles thought critical to successful cold storage solutions in general are outlined by Belzer and Southard [13]: prevention of cold-induced cellular swelling, prevention of intracellular acidosis, reduction of interstitial fluid, reduction of free radical injury, and provision of substrate for cellular energy production during reperfusion.

The UW solution represents a rational formulation designed for the in situ induction and safe maintenance of hypothermic organ protection for transplantation. The solution is clinically successful in extended protection for renal, pancreatic, and hepatic transplantation [13]. Components are included to attenuate the deleterious effects of the induction of ischemic hypothermia, maintenance of anaerobic hypothermia, and subsequent reperfusion. The UW solution incorporates the osmotically active and metabolically inactive impermeants lactobionate, raffinose, and hydroxyethyl starch. The extracellular solutions used contain a small amount of glucose, which displays organ-specific variability as an impermeant. The Stanford solution contains a higher glucose concentration, but has an additional impermeant, mannitol, and less sodium as well. These impermeant properties could account, in part, for the striking gross edema and failed protection of the extracellular cardioplegia–treated groups compared with the Stanford and UW groups. The property of reduced edema formation with the UW solution in a myocardial protection application was documented and quantified by Swanson and associates [14].

The absence of specific compounds in the extracellular fluid cardioplegia known to have a role in reduction of free radical formation or in suppression of their deleterious effects may help to explain its poor performance. In contrast, the Stanford solution contains mannitol, which is a putative free radical scavenger. The UW solution has a xanthine oxidase inhibitor, allopurinol, to reduce production of free radicals and glutathione to replenish this intracellular antioxidant [13].

A final major difference in solutions is the inclusion in the UW solution of a precursor (ie, adenosine) for high-energy compound (adenosine triphosphate) synthesis during reperfusion.

In our survey, the similarity in early survival of the two patient groups whose transplanted hearts were procured with either Stanford or extracellular fluids may be real or may not truly reflect the actual clinical effects of the different cardioplegia methods because of incomplete sampling of programs.

Assuming there is no difference in actual outcome, the disparity between the laboratory findings and the clinical findings might be reconciled by the fact that the clinical period of ischemia did not extend to the length of ischemia in our experiment, thus tending to minimize the effect of cardioplegia type. Another line of speculation to explain the dissimilar result is the different storage medium employed clinically—saline solution or a balanced saline solution analogue versus the use of the same solution as that used for the cardioplegia in our experimental model, ie, Stanford solution was the storage medium for the Stanford cardioplegia protection experimental group.

Conversely, there are also other patient, disease, or surgical factors aside from the cardioplegia technique that contribute to the overall 10% 30-day mortality and that could mask the existence of a real difference in donor cardioplegia technique.

Not all effects of poor myocardial protection would be reflected in the early or 30-day mortality figures. A sufficient number of patients for meaningful comparison of long-term outcome in regard to differing cardioplegia techniques was not yet available through the International Heart Transplant Registry (Dr Michael Kaye: personal communication, 1989).

Comparison of cardioplegic solutions for one application does not ensure that extrapolation to another situation will yield similar results. In many of the clinical reports and previous laboratory applications of these extracellular cardioplegic solutions at Emory, the solution was oxygenated. This may negate the need for an impermeant, which may be central to the effectiveness of the Stanford and UW solutions. The addition of oxygen may allow at least partial maintenance of the Na-K adenosine triphosphatase–driven osmotic gradient to minimize hypothermic cellular swelling and subsequent myocardial dysfunction. Furthermore, the favorable clinical and laboratory results with oxygenated extracellular cardioplegia were seen in standard coronary and valve operations with substantially shorter ischemic periods than encountered in clinical transplantation and in this transplant model.

These data suggest that there is no significant difference in myocardial protection between the Stanford and UW solutions if the acceptable type I error is set at the 5% level. With this sample size and the variance in these data, there is a significant risk of missing a true difference in these two protection plans. To achieve a 90% chance of avoiding a type II error in this experimental protocol, the Stanford and UW cohorts would have to have 35 individuals per group. Rather than pursuing this method of investigation further, future evaluation of Stanford and UW comparisons will be made in this laboratory using computer-aided systolic and diastolic left ventricular pressure–volume relationship studies.

It appears in light of this *basic laboratory study* that a tightly controlled comparison of the two currently clinically popular donor cardioplegia techniques shows the Stanford solution to be clearly superior to the extracellular formulations. Our *clinical survey* is not sufficiently rigorous to state that no difference in outcome between the two techniques exists. Therefore, to maximize the margin of safety in donor heart protection, it would be prudent to adhere to the Stanford regimen for distant donor heart procurement at this time.

Grateful acknowledgment is made for the generous provision of UW solution (Belzer UW-CSS) by Du Pont Pharmaceuticals, E.I. du Pont de Nemours & Co, Wilmington, DE.

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Appendix 1. Example of a Transplant Program Survey Questionnaire

Is your transplant cardioplegia the same composition as for your standard cardiac procedures? Circle: Yes No

General Category	Circle one:
A. Extracellular (Na about 100–150 mEq/L, K about 20 mEq/L)	Plasmalyte R/Isolyte S Normosol R/Ringer's lactate Normal/saline based
B. Dextrose/mannitol based (Na < 50 mEq/L, K = 20–30 mEq/L)	"Stanford" type
C. Blood cardioplegia	
D. Intracellular	"Modified Collins" type

DISCUSSION

DR ANDREW S. WECHSLER (Richmond, VA): Could we have your thoughts regarding the influence of reperfusion on your results? Do you think that what you saw could have been modified by an altered reperfusion technique, as reperfusion might not really parallel the clinical observations?

DR STEVEN R. GUNDRY (Loma Linda, CA): This is a very nice study. It echoes our opinions at Loma Linda. My associates and I have been using a crystalloid cardioplegic solution called Roe's solution developed by Benson Roe years ago. It is very much like the Stanford solution except that dextrose is used instead of mannitol. Clinically we have gone up to 8 hours 20 minutes of ischemia in 56 infant heart transplantations and have never had a graft failure due to poor perfusion and protection.

My question relates to that of Dr Wechsler. In studying this in the laboratory, did you control for the increased viscosity of UW solution by looking at amount of cardioplegia or time to administer cardioplegia? In what way do you think the reperfusion can be altered to create a clinical correlation to the centers that are using the extracellular solutions with really quite good results?

DR GOTT: In regard to reperfusion technique in our experimental model, we did take advantage of previous experimental work demonstrating that lower reperfusion pressures may be of benefit; however, this was extended to all of our experimental groups equally as the goal was to study different cardioplegic solutions and not different reperfusion methods. We reperfused at a mean arterial pressure of 50 mm Hg. We reperfused with blood at 37°C and made no effort to keep the heart arrested during the reperfusion phase.

In response to the question about the increased viscosity of UW solution, we did not determine the time necessary for the delivery of the cardioplegia, but we did note that the physical characteristics of the fluid are certainly different from the classic crystalloid solutions that we are also using. The dose of cardioplegia was indexed to the animal's mass, so that equal volumes with clinical correlation to the doses delivered in the patient setting were made.

Management of Empyema Thoracis

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Over a 5-year period, 65 adult patients with empyema thoracis were treated. The cause of the empyema was postpneumonic in 52%, postresectional in 24%, a complication of minor surgical procedures in 14%, posttraumatic in 5%, and the result of miscellaneous causes in 5%. In the postpneumonic group, infection resulted from a single aerobic organism in 41%, multiple aerobic organisms in 9%, single anaerobic organisms in 12%, and mixed aerobic-anaerobic organisms in 18%. *Peptostreptococcus, Streptococcus viridans, Staphylococcus epidermidis, Peptococcus, Staphylococcus aureus,* and diphtheroids were the most common organisms, accounting for 55% of bacterial isolates. All 34 patients with postpneumonic empyema were initially treated with drainage, which was successful in two thirds. The remainder, 12 patients, ultimately required thoracotomy. Decortication was combined with intrathoracic transposition of extrathoracic skeletal muscles in 9 patients. There was no reoperation or recurrence of infection, and thoracoplasty was avoided; residual spaces were filled by the transposed muscle.

(Ann Thorac Surg 1990;50:355–9)

Despite the widespread availability of antibiotics and a declining incidence [1], empyema thoracis remains a serious problem. The present series of 65 patients represents a typical patient population of empyema treated at a large tertiary-care facility with an associated community-based referral.

The approach was conventional and included initial drainage followed by thoracotomy if the empyema failed to resolve. Although there are reports on the merits of early decortication [2], in most studies the conventional approach has been used. We found intrathoracic transposition of extrathoracic skeletal muscles to be very effective as an adjuvant to decortication in postpneumonic empyema. The transposed muscle filled all residual intrathoracic spaces after decortication, thereby avoiding the need for thoracoplasty.

For editorial comment, see page 343.

Material and Methods

Over a 5-year period 65 adult patients, 60 men and 5 women, with empyema were referred to the Thoracic Surgical Service of the Health Sciences Center, Winnipeg. The Health Sciences Center is a major tertiary-care center and also serves a large population of patients from the surrounding central area of the city. All patients with suspected empyema in the Center are referred to the Thoracic Surgical Service. The patients included in this series all had pleural effusion with an elevated white blood cell count consisting predominantly of granulocytes or had bacterial organisms demonstrated on Gram stain or culture. Parapneumonic effusions that did not meet these criteria are not included in this review. All pleural fluid specimens were routinely cultured for fungi, acid-fast bacilli, and bacteria under aerobic and anaerobic conditions.

The patient population was divided into five groups as described by de la Rocha [3]. Group 1 consisted of patients with postpneumonic empyema (PPE). Group 2 consisted of patients in whom empyema developed after pulmonary resection. Group 3 consisted of patients in whom empyema developed as a complication of minor thoracic surgical procedures such as thoracentesis and chest tube insertion. Group 4 included patients with empyema secondary to blunt or penetrating trauma to the chest, and group 5 consisted of a small group of patients with miscellaneous causes for empyema.

The surgical approach used in patients with PPE, who constituted the majority of patients, was standardized and tended to progress in the following sequence: chest tube insertion, rib resection with or without open thoracostomy, and thoracotomy. Rib resection differed from open thoracostomy only in the initial management after operation. A short segment of rib was resected at the most dependent portion of the empyema. The cavity was fully evacuated, and loculations were broken down. A large drainage tube (36F) was placed, securing an airtight seal. For the first 4 to 5 postoperative days, drainage with underwater seal was used to aid reexpansion of the lung and to avoid the potential complication of complete pneumothorax due to incomplete pleural symphysis. Thereafter, in the presence of a residual cavity, the tube was cut to facilitate continuous passive drainage with once-daily irrigation with sterile normal saline solution. The patients were discharged and reassessed with chest roentgenogram or sinogram every 4 to 6 weeks. Failure to progress with no decrease in size of the cavity, development of septic complications, or bronchopleural fistula was considered as indication for thoracotomy.

In patients with PPE we modified the standard posterolateral thoracotomy customarily used for decortication.

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Table 1. Causes of Empyema

Group	Cause of Empyema	No. of Patients (%)
1	Postpneumonic	34 (52)
2	Postresectional	16 (24)
3	Minor surgical procedures	9 (14)
4	Posttraumatic	3 (5)
5	Miscellaneous	3 (5)
Total		65

The skin incision was completed down to but not through muscle. The skin and subcutaneous tissues overlying the muscle caudal to the incision were then dissected off the lateral surface of latissimus dorsi. This was continued until the broad fibrous insertion into the spinous processes was identified. At this level, the attachments were cut and the muscle was detached from the iliac crest. The medial surface of latissimus dorsi was detached from the chest wall and mobilized back to the level of the skin incision. The chest cavity was then opened through the bed of the sixth rib. After decortication, the condition in each patient was assessed with regard to the bulk of muscle required to obliterate potential problem spaces. If the lung reexpanded to fill the entire thoracic cavity and there was no major bronchopleural fistula, the chest was closed, and latissimus dorsi was reattached to the spine and iliac crest with five or six interrupted sutures. If there were substantial areas on the anterior, lateral, or posterior aspects of the lung that failed to reexpand or if a large bronchopleural fistula was present, the remainder of latissimus dorsi was mobilized, leaving it attached to the humerus. If an additional potential space was identified in the apex of the thorax, the serratus anterior was detached from the chest wall and lateral border of the scapula, with the thoracodorsal neurovascular trunk carefully preserved. The midportion of the third rib was resected, and the muscles were transposed into the thoracic cavity either on top of or around the lateral aspects of the lung. This immediately stopped all air leaks from the decorticated surface of the lung and proved enough bulk to fill the residual spaces.

Management of the remaining four groups is described briefly to contrast the difference with the PPE patients.

Table 2. Type of Infections in Postpneumonic Empyema

Infection	n (%)
Single aerobe	14 (41)
Single anaerobe	4 (12)
Mixed aerobic-anaerobic	6 (18)
Multiple aerobes	3 (9)
Multiple anaerobes	0
Culture negative	6 (18)
Fungal	1 (2)
Total	34

Table 3. Frequency of Organisms in Postpneumonic Empyema

Organism	n (%)
Peptostreptococcus	5 (12)
Staphylococcus epidermidis	5
Streptococcus viridans	4 (10)
Peptococcus	3 (7)
Diphtheroids	3
Staphylococcus aureus	3
Streptococcus pyogenes	2 (5)
Haemophilus influenzae	2
Fusobacterium nucleatum	2
Acinetobacter	2
Bacteroides	2
Enterobacter aerogenes	1 (2)
Klebsiella pneumoniae	1
Pseudomonas	1
Microaerophilic streptococci	1
Micrococcus species	1
Steptococcus pneumoniae	1
Clostridium species	1
Anaerobic gram-positive cocci	1
Anaerobic gram-positive bacilli	1
Total	42

Results

The causes of empyema are shown in Table 1. Postpneumonic empyema and iatrogenically induced empyema (groups 2 and 3) accounted for 90% of cases. The type of infections that occurred in the 34 patients with PPE are shown in Table 2. Table 3 shows the offending organisms in decreasing frequency of occurrence. Pure aerobic infection accounted for 50% of cases, and infection with a single organism was by far the most common form of PPE. The organisms were of a diverse nature and generally reflected the predominant organisms held to be responsible for the underlying pneumonia. Anaerobic organisms were involved in 30% of infections, more frequently in association with an aerobic organism. All 4 patients with pure anaerobic infection had infection with either *Peptostreptococcus* or *Peptococcus*, and no pure multiple anaerobic infection occurred. The predominance of these two pathogens was also reflected in the patients with mixed aerobic-anaerobic infections, with 4 of 6 patients having one or the other grown on culture. One patient in the mixed infection group had two, 3 patients had three, and 2 patients had four organisms grown on culture of the pleural fluid.

Patients with PPE were treated as follows. Seventeen patients had a chest tube placed as the initial step in their management. All but 1 required rib resection, and in 14 others this was the initial procedure. Three patients required open thoracostomy by creation of a pleurocutaneous window as described by Eloesser [4] to achieve better control of the septic process. Two of these and 10 others ultimately required decortication with muscle transposition. In 3 patients, muscle transposition was not required and the mobilized lower half of latissimus dorsi was reattached. One patient required left lower lobectomy with decortication and muscle transposition. No reoperation, recurrence of infection, or death occurred in this group of patients. Preoperative and postoperative roentgenograms of 2 illustrative patients are shown in Figures 1 and 2.

Patient 1

Figure 1A shows the preoperative chest roentgenogram of a 57-year-old man with a known history of idiopathic pulmonary fibrosis who had PPE. After decortication, it was quite apparent that his fibrotic lung would not fill the thoracic cavity. Serratus anterior was placed in the apex of the thorax, and latissimus dorsi was placed over the lateral surfaces of the lung. The fourth to seventh ribs were resected to ensure that all potential spaces were obliterated (Fig 1B shows the chest roentgenographic appearance 3 months later). Therefore, we were able to leave the first three ribs intact to provide support for the shoulder. Functionally, abduction was limited to 90 degrees, but otherwise range of motion was normal.

Patient 2

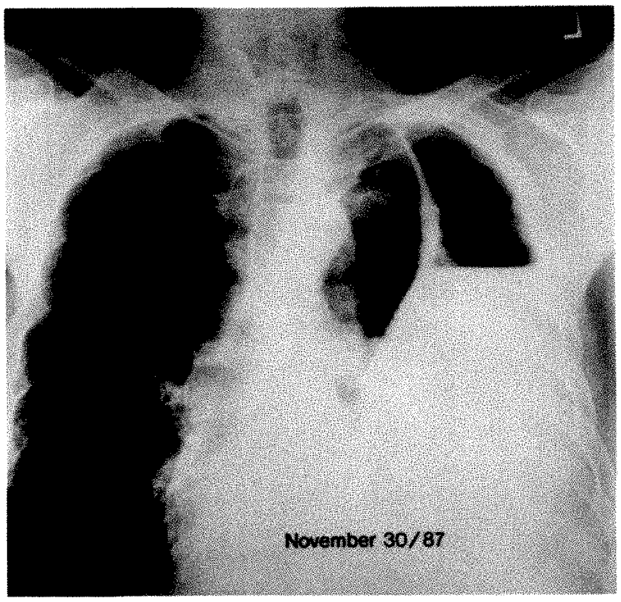
Figure 2A shows a preoperative chest roentgenogram of a previously healthy 55-year-old man. The PPE was predominantly in the lower half of the posterior aspect of the chest, and latissimus dorsi was required to obliterate the empyema cavity and close the bronchopleural fistula. Figure 2B shows the result 6 weeks later. The patient's shoulder has full range of motion.

Treatment of Other Types of Empyema

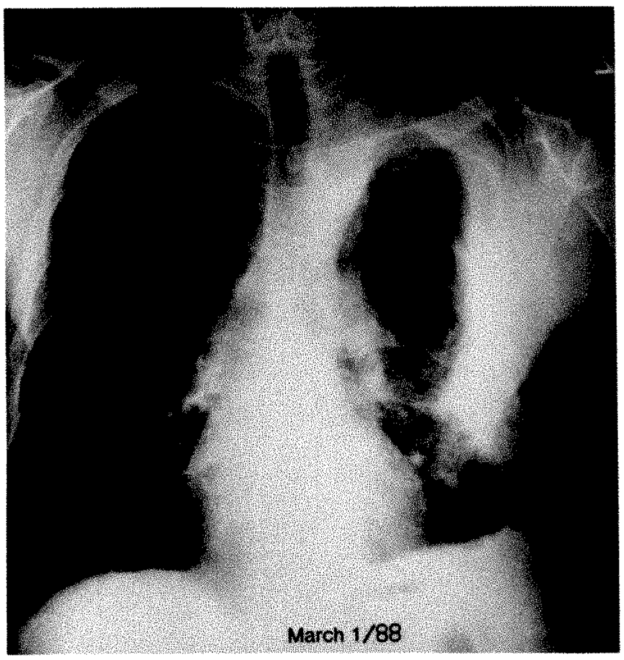
Sixteen patients with postresectional empyema (9 acute and 7 chronic) were treated. In the acute group, 3 patients had pneumonectomy and 6 had lobectomy as their initial procedure. In the chronic group, consisting of 6 pneumonectomy patients and 1 lobectomy patient, all had had operations from 1 to 29 years earlier. Treatment was varied and complicated and therefore had to be individualized for each patient. Drainage with or without endoscopic application of fibrin sealant was all that was required in patients who had undergone lobectomy. Urgent drainage in the pneumonectomy patients usually controlled the sepsis and allowed assessment of the stump under elective circumstances. Two fistulas in this group were sealed successfully with fibrin sealant. Surgical closure was attempted in 4 patients and was successful in 2. All patients required multiple operations. Two patients in the acute group and 1 in the chronic group died, for an overall 19% operative mortality rate in the postresectional empyema group.

Nine patients with empyema as a complication of minor thoracic surgical procedures were treated. Seven patients had gram-positive organisms (*Staphylococcus aureus*, *Staphylococcus epidermidis*, and diphtheroids), and 2 patients who had lengthy previous hospitalizations for serious medical problems had a gram-negative organism on pleural fluid culture. In 3 patients, pleural sepsis was controlled with rib resection alone; 4 subsequently required decortication, and 1 of the 4 died. Two patients died before anything could be done, resulting in an overall mortality of 33% after inadvertent iatrogenic infection of the pleural space.

Three patients had empyema secondary to blunt or penetrating trauma to the chest. Two had penetrating trauma, and 1 had blunt thoracic trauma. All had hemo-



A



B

Fig 1. (Patient 1.) A 57-year-old man with known idiopathic pulmonary fibrosis had postpneumonic empyema associated with bronchopleural fistula (A). Serratus anterior and latissimus dorsi were required to obliterate the apical and posterolateral empyema cavity (B).

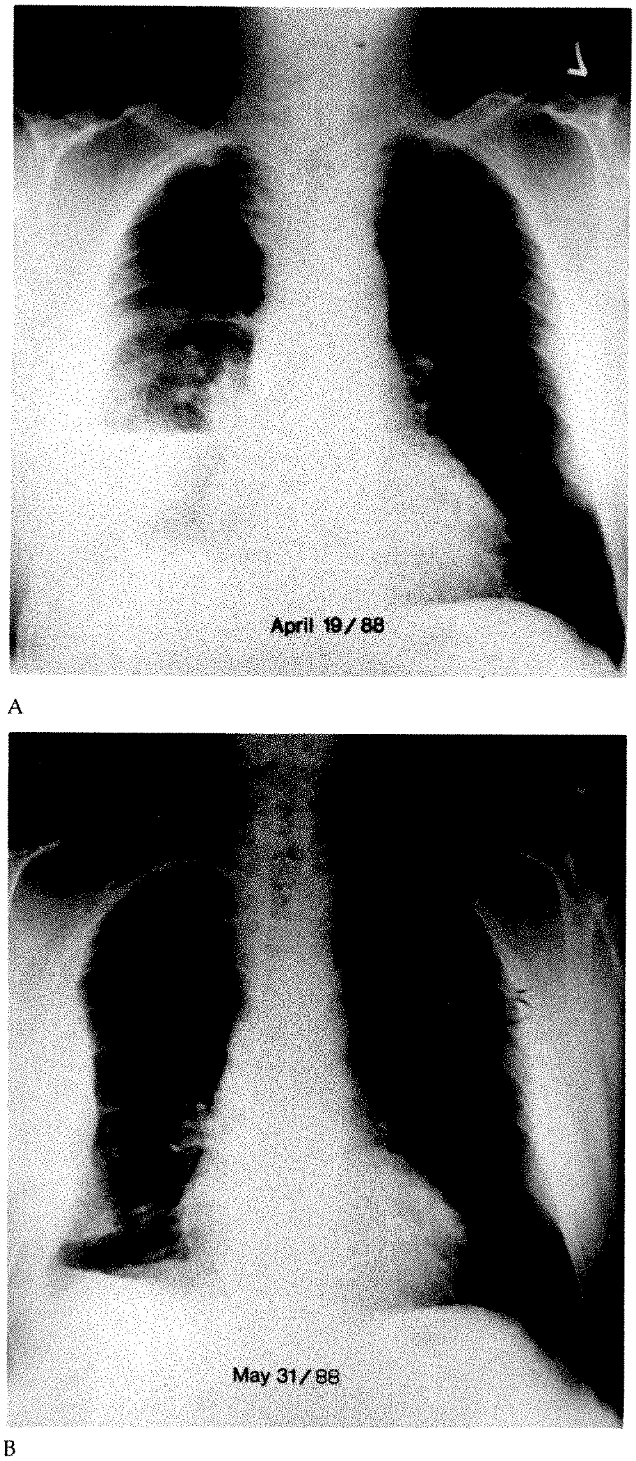


Fig 2. (Patient 2.) A 55-year-old previously healthy man had postpneumonic empyema associated with a bronchopleural fistula (A). Latissimus dorsi was required to obliterate the posterolateral empyema cavity (B).

thorax, initially managed by chest tube insertion. Serial roentgenograms showed residual organizing hemothorax and partial lung collapse associated with intermittent low-grade fever and mild elevation of the white blood cell count. All patients were operated on acutely, with evacuation of the hematoma and reexpansion of the lung. Culture of the hematoma yielded organisms.

The final group of patients includes 3 patients who had miscellaneous causes for empyema. One patient was a diabetic with *S aureus* septicemia complicated by empyema. One patient had an obstructing carcinoma of the right lower lobe treated by radiotherapy and subsequently complicated by empyema. Both were successfully managed with rib resection. The last patient had gastric perforation secondary to a paraesophageal hernia, and the infection was treated at the time of thoracotomy.

Comment

The objectives of surgical treatment of empyema thoracis are twofold. The infected material must be evacuated and the lung reexpanded. Reexpansion is of paramount importance, as a residual space will almost certainly lead to reinfection. Appropriate long-term antibiotic coverage is also required to control the local and systemic infection.

Postpneumonic empyema constituted the leading cause of empyema in this series of patients. Approximately half of the cases resulted from infection by aerobes, one fourth from anaerobes, and one fourth from mixed aerobic-anaerobic infection. This pattern of infection was previously reported by Varkey and colleagues [5]. The six most prevalent organisms, accounting for 53% of isolates, were common gram-positive organisms not often considered pathogens. In 6 patients who had been treated with antibiotics before their first thoracentesis, cultures failed to grow an organism.

All but 1 of the 34 patients required rib resection under intercostal or general anesthesia. This has also been the experience of other investigators [6], although there is some controversy about the methods of drainage and the need for procedures other than chest tube drainage [7–9]. In 3 patients, open thoracostomy was required to gain better control of the septic process. A protocol of daily irrigations with normal saline solution and continuous passive drainage for up to 3 months resulted in complete resolution of the PPE in 65% of patients.

Twelve patients required thoracotomy, and 9 required muscle transposition. Intrathoracic transposition of extrathoracic skeletal muscles is not new. In 1949, Maier and Luomanen [10] described pectoral myoplasty for obliteration of tuberculous empyema cavities after thoracoplasty. More recently, muscle transposition has also proved very useful in the management of postresectional empyema, especially postpneumonectomy empyema [11–13]. In the series of Pairolero and co-workers [11], 11 of 31 patients had bronchopleural fistula with residual lung in the hemithorax after muscle transposition. Two of these were the result of chronic empyema.

After decortication, the lung is often contracted, with loss of compliance owing to extensive inflammation and fibrosis. The time-honored approach to this dilemma is thoracoplasty. Although good results have again recently been reported with thoracoplasty [14] and interesting innovations have been described [9, 15], thoracoplasty still is problematical. It is rarely considered a one-stage procedure with decortication. The combined procedure can be very lengthy, which can be deleterious for patients.

Second, it is difficult to predict preoperatively or even in the immediate postoperative period whether a patient will require thoracoplasty. The result also can be cosmetically disfiguring and lead to chronic spine and shoulder difficulties. Therefore, based on the favorable and encouraging results reported by Pairolero and co-workers [11], we selected muscle transposition as an alternative to thoracoplasty in the management of PPE. Using the criteria described in the Material and Methods section, muscle transposition was required in 75% of our operative cases. This relatively high proportion may be explained by the initial method of management. These cases tended to be decorticated late, and many irreversible changes such as localized fibrosis may have been present by then. Even in these cases, we were able to avoid thoracoplasty by use of muscle transposition.

The treatment of postresectional empyema, especially postpneumonectomy empyema with bronchopleural fistula, remains a difficult challenge. Nine of the 16 patients in our series had postpneumonectomy fistula. Immediately after diagnosis, these patients had open thoracostomy. Attempts were made to close small fistulas with fibrin sealant and, if this was successful, the patients underwent the second stage of the procedure of Clagett and Geraci [16] later. In the remainder, the fistula was too large for this form of management. Two available options were used in our patients. These include thoracoplasty with muscle transposition [13], which is often combined with myoplasty [17] in a direct attempt to close the fistula. The alternative is transpericardial suturing of the residual stump [18], which is particularly applicable if there is a long residual stump [19]. In the former method, we used intercostal muscle bundles to close the bronchopleural fistula, and extrathoracic muscles were placed medial to the residual intercostal muscles to obliterate the pneumonectomy space completely. Based on our limited experience, we believe that this should be tried first and that transpericardial suturing should be reserved for failures.

As shown by this series, iatrogenic infection of a sterile pleural effusion is associated with substantial morbidity and mortality. In this series, one third of patients required rib resection alone, one third required decortication, and one third died early in the course of their infection, which reflects the serious underlying illnesses that have prompted hospital admission for these patients.

Hemothorax after blunt or penetrating trauma is very frequent and can usually be managed adequately with chest tube drainage. If residual hemothorax is associated with partial lung collapse, fever, and leukocytosis, these patients should be operated on promptly. The blood clot is readily evacuated, and the lung easily reexpands. The postoperative course of these patients is short; the evacuated material will usually be sterile but may grow an organism, especially if the trauma was penetrating.

This series of patients demonstrates that closed chest tube drainage alone is usually unsuccessful and virtually all patients will require an operative drainage procedure. We found rib resection under intercostal or general anesthesia to be very effective. Use of extrathoracic muscle transposition as an adjuvant to decortication for PPE allows immediate closure of bronchopleural fistula, is theoretically beneficial in dealing with residual sepsis by obliterating potential spaces with healthy vascularized tissue, and avoids some of the deforming and disabling consequences of thoracoplasty.

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Flow Capacity of the Human Retrograde Internal Mammary Artery: Surgical Considerations

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The diastolic flow of the retrograde internal mammary artery (IMA) was calculated in 30 patients and compared with the expected coronary flow of the left ventricle and that of specific branches. Arterial pressure and free flow were measured in the proximal and distal IMA as well as in the superior epigastric and musculophrenic arteries. Systolic and mean arterial pressure were significantly higher in the proximal IMA than in any other site, but diastolic pressure was comparable. Overall and diastolic antegrade IMA flows (77 ± 6 and 44 ± 3 mL/min) were significantly greater than the retrograde flows through the distal IMA (18.5 ± 2 and 11.5 ± 1 mL/min), musculophrenic artery (13.3 ± 1 and 7.9 ± 1 mL/min), and superior epigastric artery (5.3 ± 0.4 and 3.1 ± 0.2 mL/min). Only patient-size–related variables correlated significantly with retrograde IMA flow. Diastolic retrograde IMA flow represented 8.5% ± 0.6% of the expected left ventricle coronary flow and in 12 patients (40%) was greater than the expected flow of at least one posteroinferior coronary artery. Based on these data, the retrograde IMA may adequately perfuse the posterior descending or other posterolateral coronary branches in select patients. Previous measuring of the retrograde flow is mandatory.

(Ann Thorac Surg 1990;50:360–6)

Internal mammary artery (IMA) graft has proved to be clearly superior to saphenous vein graft in the surgical treatment of coronary artery disease. Its excellent long-term patency determines a more complete protection against further ischemic events and a better late survival. Adequacy of IMA flow to perfuse myocardium has been experimentally and clinically demonstrated. This is true not only for single IMA grafts, either free or pedicled, but also for sequential IMA grafts. With a view to extend the use of IMA to distant coronary vessels, usually not amenable to revascularization with antegrade pedicled grafts, the distally based "inverted" or "retrograde" IMA graft was introduced [1–3].

Nevertheless, flow characteristics through this kind of graft could be remarkably different from those of the antegrade graft. Retrograde IMA free flow measurements in previous clinical experiences resulted in disappointingly small absolute values, well below those usually found with the antegrade IMA [3, 4]. The arterial pulse in the retrograde IMA is delayed, however, as compared with that in the ascending aorta and the antegrade IMA, which could increase blood flow delivery during diastole and thus result in enhanced myocardial perfusion.

Because the decision to use IMA in either antegrade or retrograde mode must be made before the free flow in both directions can be measured, it would be interesting to know in advance the adequacy of retrograde flow. Therefore, we quantified the free flow of the distal stub of the IMA and correlated it with different somatic and hemodynamic variables to discover the presence of any predictive value. As left ventricular myocardium is perfused almost exclusively in diastole [5], the diastolic component of the retrograde IMA flow was calculated and compared with the expected flow of the posteroinferior coronary branches. Our intention was to determine the adequacy of the retrograde IMA to be used as a bypass graft to distant coronary vessels not reachable by the proximally based pedicled IMA.

Material and Methods

Antegrade and retrograde free flows were measured in 30 patients (28 men and 2 women) in whom the left IMA was used for coronary grafting (28 single and two sequential IMA grafts) as an antegrade pedicled graft. All patients underwent isolated myocardial revascularization, being free of associated valve disease or left ventricular hypertrophy. The existence of occlusive arterial disease involving the supraaortic and aortoiliac vessels was sought by anamnesis, physical examination, and Doppler echocardiography when necessary. Patients' weight, height, and body surface area were recorded in every case. Before anesthesia was induced, appropriate catheters were placed to monitor the right radial artery pressure, central venous pressure, pulmonary artery pressure, and cardiac output. When necessary, preload, afterload, or both were adequately modified by infusion of either crystalloids or nitroglycerin to keep the hemodynamic conditions as stable as possible throughout the study phases. All data were recorded and stored in a Siemens-Sirecust 1281

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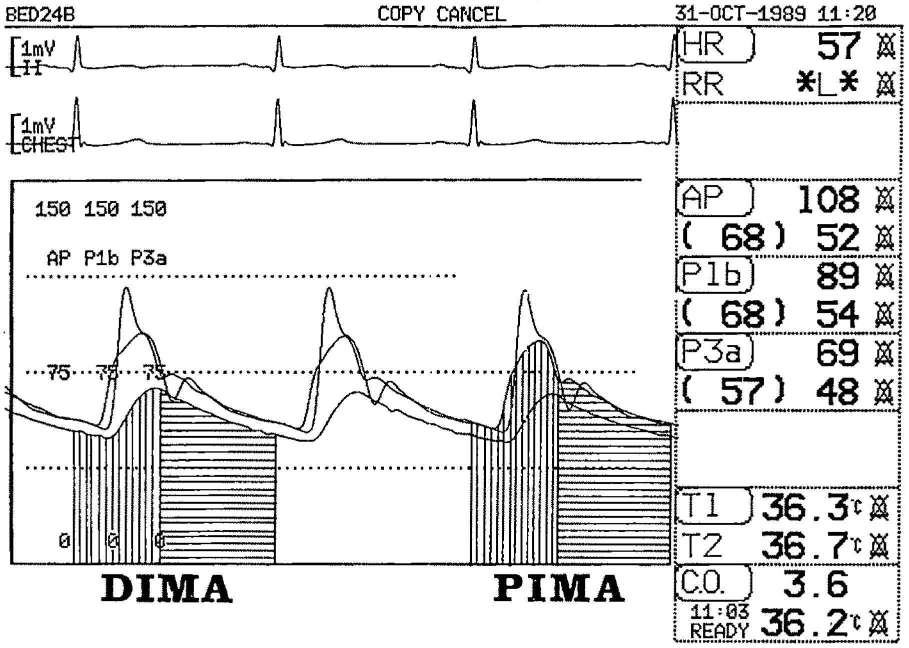

Fig 1. Simultaneous recording of the electrocardiogram and pressure waves of the radial artery (AP)*, proximal internal mammary artery* (PIMA) (P1b) *and distal IMA* (DIMA) (P3a). Shaded areas *correspond to* systole (vertical lines) *and diastole* (horizontal lines) *of the distal and proximal IMA in two separate cardiac cycles. Absolute values of the systolic, diastolic, and mean (in parentheses) pressures are showed on the right.*

multichannel monitor (Siemens Medical Electronics, Danvers, MA).

The left IMA was completely dissected free from its origin to its bifurcation into superior epigastric and musculophrenic arteries, as well as the first 2 cm of these branches. It was then generously sprayed with diluted papaverine (30 mg in 20 mL of saline solution) and wrapped in a papaverine-soaked gauze to prevent arterial spasm. After systemic heparinization (3 mg/kg) and before cannulation of the aorta and right atrium, the IMA was divided 1 cm proximal to its bifurcation. One milliliter of diluted papaverine was then injected into both arterial ends to reverse any possible spasm, although no attempts were made at either hydrostatic or instrumental dilation.

Flow measurements were made under conditions of clear and stable bloodstream, with the sternal halves maintained as close as possible to avoid IMA distortion. During each flow measurement, radial artery pressure (systolic, diastolic, and mean) and heart rate were registered, and cardiac output was calculated. The following recordings and measurements were made sequentially:

1. Internal IMA diameter was calibrated by graduated probes.
2. Free antegrade and retrograde IMA flows were measured simultaneously for 1 minute.
3. Both ends of the IMA were cannulated with 20-gauge catheters (Cathlon IV, Critikon, Creteil-l'Echat, France) and then connected to pressure transducers. The electrocardiogram and the pressure waves of the radial artery, proximal IMA, and distal IMA were recorded simultaneously (Fig 1).
4. The musculophrenic branch was temporarily occluded and a simultaneous recording of the electrocardiogram, radial artery, proximal IMA, and superior epigastric artery pressure waves was obtained. Then we clamped the superior epigastric branch and obtained a simultaneous recording of the electrocardiogram and the pressure waves from the radial artery, proximal IMA, and musculophrenic artery.
5. Retrograde free flows through the musculophrenic and superior epigastric arteries were then sequentially obtained for 1 minute after the other terminal branch was occluded.

The surface area under the different pressure waves of the IMA system (proximal IMA, distal IMA, musculophrenic artery, and superior epigastric artery) was measured by planimetry in five consecutive cardiac cycles, and a mean value was calculated. Then we proceeded identically with the diastolic portion of the pressure waves, taking as references the end of the T wave and the peak of the following R wave in the simultaneous electrocardiogram recording (Fig 1). Thus, a diastolic/overall pressure area ratio was assigned to each arterial site. The product of this ratio times the corresponding absolute flow value was considered the diastolic flow component (DFC) of that arterial site. For purposes of the study, we considered IMA diameter to remain unchanged throughout the cardiac cycle. This assumption might overestimate the DFC, as a reduction in IMA diameter during diastole is to be expected. The delay between the onset of systole, determined by the peak of the R wave and the beginning of the ascending slope in the corresponding pulse pressure wave, was measured at each arterial level.

The left ventricular mass and the expected left ventricular coronary flow (LVCF) were calculated in each patient by the method described by Schlant and associates [5], in the absence of clinically significant ventricular hypertrophy or dilatation. Starting from the preoperative coronary arteriography of each patient, a myocardial value was assigned to every left posteroinferior coronary branch

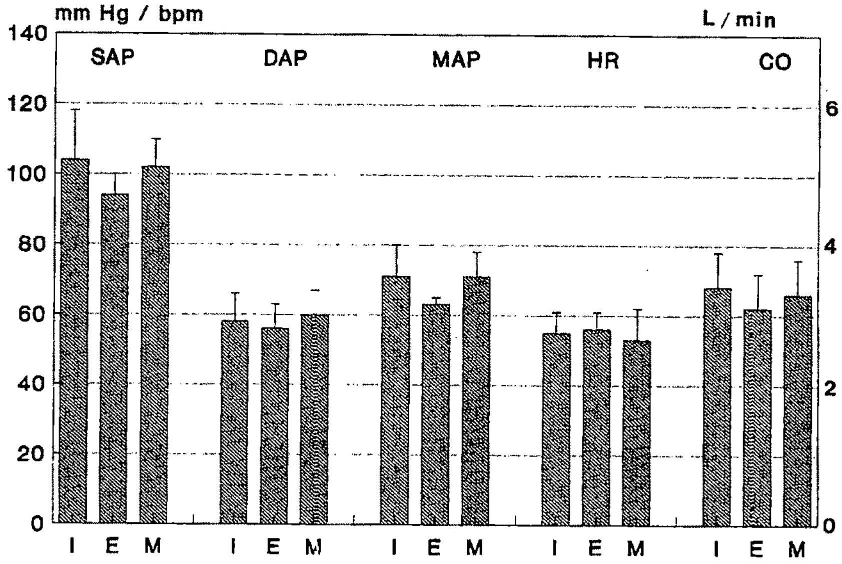

Fig 2. Hemodynamic variables recorded during the three phases of flow measurement: proximal and distal internal mammary artery ends (I), superior epigastric artery (E), and musculophrenic artery (M). (CO = cardiac output; DAP = diastolic arterial pressure; HR = heart rate; MAP = mean arterial pressure; SAP = systolic arterial pressure.)

using the myocardial perfusion score proposed by Friesinger and colleagues [6]. The expected blood flow (EBF) supplied by specific coronary branches was calculated by applying the formula: EBF = LVCF × myocardial value/15, where 15 corresponds to the myocardial value of the entire left ventricle. In this manner, we calculated the EBF of the posterior descending artery and that of the coronary vessels supplying the posterolateral aspect of the left ventricle, termed as first, second, and third posterolateral arteries. Denomination was made according to their location in the distal (near the posterior descending artery), median, or proximal segment of the posterolateral area, respectively, regardless of their origin in the circumflex or right coronary arteries. Thus, we could analyze approximately the sufficiency of the retrograde IMA flow to match the EBF of specific coronary vessels.

Statistical comparison between the different variables (presented as the mean ± the standard error of the mean) was made by Student's t test for paired and unpaired data as appropriate. A correlation analysis between each arterial flow and different somatic (weight, height, body surface area), anatomical (IMA size), and hemodynamic variables (systolic, diastolic, and mean radial pressures and cardiac index) was also performed; p values less than 0.05 were considered statistically significant.

Results

No patient had evidence of occlusive arterial disease involving either the supraaortic or the aortoiliac areas, nor had any patient had previous abdominal incisions. Mean age of the group was 57 ± 2 years (range, 36 to 70 years). Mean weight, height, and body surface area were 73 ± 2 kg (range, 54 to 95 kg), 164 ± 1 cm (range, 151 to 176 cm), and 1.7 ± 0.02 m^2 (range, 1.48 to 2.04 m^2), respectively. The mean IMA diameter was 1.6 ± 0.04 mm, and in only one third of the patients was it 2 mm or greater.

Hemodynamic conditions remained unchanged throughout the different phases of the study (Fig 2). The systolic and mean pressures of the radial artery and proximal IMA were significantly higher than the systolic and mean pressures at other sites ($p < 0.005$ and $p < 0.05$, respectively). Diastolic pressures were comparable at all arterial sites (Fig 3). There was a significant increase ($p < 0.01$) in the mean delay in pulse pressure between the proximal IMA (124 ± 6 ms) and the distal IMA (201 ± 8 ms). The superior epigastric and musculophrenic arteries showed a mean pulse delay similar to that found in the distal IMA.

Different arterial blood flows are shown in Figure 4. Free antegrade IMA flow was 77 ± 6 mL/min (range, 37 to 165 mL/min), and its DFC was 44 ± 3 mL/min (range, 23 to 91 mL/min). The free retrograde IMA flow (18.5 ± 2 mL/min; range, 10 to 34 mL/min) and its DFC (11.5 ± 1 mL/min; range, 6 to 21 mL/min) were significantly smaller than the antegrade flows ($p < 0.001$). The retrograde flow of the superior epigastric (overall, 5.3 ± 0.4 mL/min; DFC, 3.1 ± 0.2 mL/min) and musculophrenic arteries (overall, 13.3 ± 1 mL/min; DFC, 7.9 ± 1 mL/min) were even smaller. Overall flow and DFC were both significantly greater ($p < 0.001$ and $p < 0.01$, respectively) in the musculophrenic than in the superior epigastric artery, although the diastolic/overall pressure area and flow ratio was identical. This ratio was slightly but statistically greater in the retrograde IMA than in the antegrade IMA (0.60 ± 0.01 and 0.57 ± 0.01, respectively; $p < 0.05$).

When the correlations between IMA flows and different somatic data were analyzed, only the distal IMA and musculophrenic backflows correlated significantly with variables related to patients' size ($p < 0.01$ for weight and $p < 0.05$ for height and body surface area). With regard to hemodynamic variables, we found significant correlation only between diastolic and mean arterial pressures and antegrade IMA flow ($p < 0.05$). When flows were correlated among themselves, the only significant correlation was between backflow of the distal IMA and that of the musculophrenic artery ($p < 0.05$). In every instance in which a variable correlated significantly with an overall

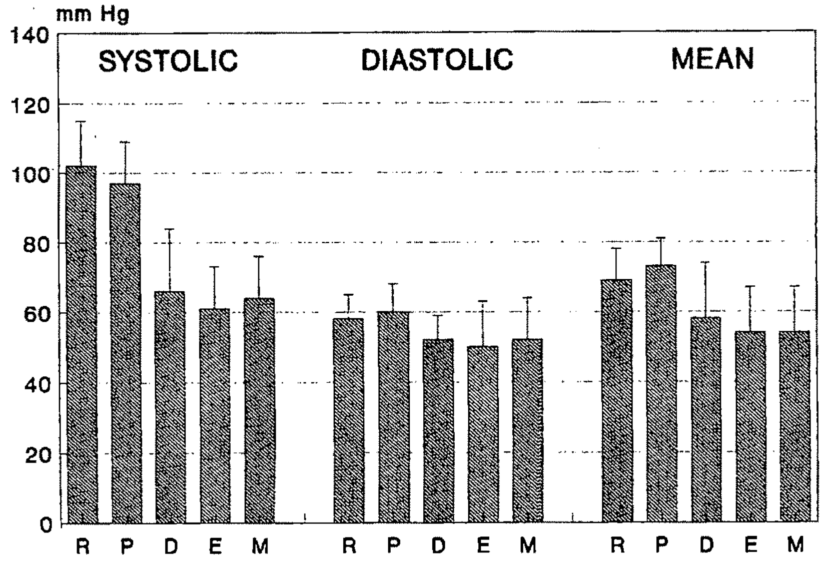

Fig 3. Comparison of the pressure values recorded at different arterial sites. (D = *distal internal mammary artery;* E = *epigastric artery;* M = *musculophrenic artery;* P = *proximal internal mammary artery;* R = *radial artery.)*

flow, it also correlated significantly with its diastolic components.

Mean left ventricular mass was 160 ± 4 g (range, 119 to 209 g), and the expected LVCF was 128 ± 3 mL/min (range, 95 to 167 mL/min). The mean overall retrograde IMA flow represented 14.4% ± 0.9% of the expected LVCF (range, 8% to 24%); it was more than 10% in 21 patients (70%) and more than 20% in only 6 (20%). When only the diastolic component of the retrograde IMA was considered (mean, 8.5% ± 0.6% of the LVCF; range, 5% to 15%), only 12 patients (40%) reached 10% of LVCF and none was more than 20%.

A mean of 2.9 ± 0.2 coronary branches supplied the posteroinferior left ventricular area, including the posterior descending artery. Twenty-five patients had a first posterolateral, 18 had a second posterolateral, and 16 had a third posterolateral artery. According to the myocardial perfusion score, the mean percentage of LVCF corresponding to each one of these vessels was 12.8 ± 0.4 for the posterior descending artery and 11.8 ± 1.2, 8.4 ± 0.5, and 8.3 ± 0.5 for the first, second, and third posterolateral arteries, respectively. Thus, the DFC of the retrograde IMA was greater than the EBF of at least one of these vessels in 12 patients (40%). Overall, a mean of 1 ± 0.2 posteroinferior coronary branches per patient were theoretically suitable for grafting with the retrograde IMA.

Comment

Use of the IMA in myocardial revascularization is now identified as an important factor influencing early and late results [7, 8]. Its structure and adaptability condition a more physiological myocardial perfusion than do the venous grafts [9, 10]. In addition, the limited involvement of the IMA by the pathological phenomena responsible for late vein graft failure determines its excellent long-

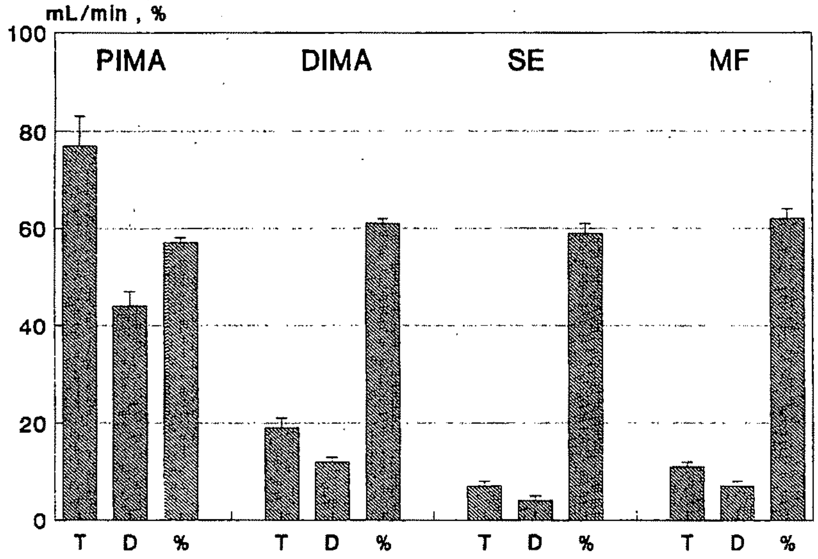

Fig 4. Absolute blood flow values, overall (T) *and diastolic* (D), *and percentage of diastolic flow component* (%) *of the different flows.* (DIMA = *distal internal mammary artery;* MF = *musculophrenic artery;* PIMA = *proximal internal mammary artery;* SE = *superior epigastric artery.)*

term patency [11, 12]. On the other hand, the greater technical complexity inherent to IMA grafting seems to carry neither associated morbidity nor additional operative risk [13]. Use of the retrograde IMA should offer better revascularization to inferior and posterolateral coronary branches not amenable to grafting with the length-limited proximally based IMA. Thus, the retrograde IMA should be considered exclusively as an alternative to other arterial grafts, which may be more technically demanding or increase the complexity of the operation.

Experimental studies by Florian and co-workers [14], Folts and associates [15], and, more recently, Von Segesser and colleagues [16] clearly demonstrated that the flow of the retrograde IMA was sufficient to perfuse adequately every myocardial region in the dog. Despite this evidence, reports of use of retrograde IMA in humans have been anecdotal only. Initial clinical experience began with Kolesov and Petukhov [1] in the late 1960s. They anastomosed, without cardiopulmonary bypass, the retrograde left IMA to the distal left anterior descending artery in several patients with immediate clinical success. Previous experimental work by these investigators showed the retrograde IMA pressure (range, 22 to 75 mm Hg) to be sufficient to perfuse the left anterior descending artery distal to a complete occlusion. They found this graft especially indicated when distal coronary segments were to be grafted, if the left IMA was short, or if this artery was damaged proximally during graft preparation. More recently, Goiti and Smith [2] and Livi and co-workers [3] each reported 1 case of retrograde right IMA grafting to the posterior descending artery, with indirect evidence of adequate flow. Nevertheless, Livi and co-workers [3] and, more recently, Cohen and associates [4] issued a word of caution about the poor retrograde IMA flow observed in humans, judged in most instances as not suitable for a secure revascularization of major coronary vessels.

Although there is no agreement as to the smallest IMA free flow required to warrant perfusion to every myocardial area, it should exceed the expected flow demand of the vascular bed to be perfused. Minimal recommended antegrade IMA free flows average 50 to 60 mL/min for single grafts and about 150 mL/min for sequential ones, both in basal conditions [17, 18]. Other investigators require flows greater than 120 mL/min after either IMA dilation or sternal approximation [19]. Nevertheless, the main determinant of the effective flow in the grafted IMA is the runoff in the involved coronary bed and not the free IMA output [19]. In fact, when the flow through the performing antegrade IMA graft is assessed by different methods, values are consistently smaller, about 35% to 45% of the previously measured free flows [17, 19, 20]. Free flows recorded in the retrograde IMA have been essentially smaller than those in the antegrade IMA. Thus, in 32 patients studied by Cohen and co-workers [4], mean retrograde flow was 24 mL/min (32% of antegrade flow), although the possibility of some underassessment owing to more difficult measuring was reported. Based on this finding, they recommended that the IMA not be used in the retrograde position. In contrast, the previously mentioned experimental studies [14–16] proved that, with absolute flow values comparable with those noted in humans, the retrograde IMA was appropriate for supplying certain myocardial regions. Moreover, the significant flow reduction noted in the already performing antegrade IMA grafts (mean effective flow, 40% of the previously measured free flow [17, 19, 20]) appears to be smaller in the case of the retrograde IMA graft (effective flow was 62% of the free flow in the study of Folts and associates [15]). This could be explained by a more advantageous left ventricular perfusion by the retrograde IMA owing to the arterial pulse delay.

Our study was designed to quantify the magnitude of the diastolic component of the retrograde IMA flow, its determinants, and its adequacy to perfuse some myocardial regions. Even though intraoperative measurement of the IMA free flow is subject to some criticism because of the influence of conditions such as arterial spasm or distortion [15, 21], it still remains the most widely used method of determining graft suitability. A good correlation has been demonstrated between free flow and maximal flow in the grafted IMA; the latter was measured after administration of isoproterenol [22]. With these objections in mind, free flow measurement is strongly recommended for both antegrade and especially retrograde IMA grafting [2, 3, 15, 18]. Mean antegrade IMA flow in our patients was in the lower range of that reported by other investigators [17, 19, 23], although the hemodynamic conditions were comparable. This could be a consequence of differences in patient size, but we could not confirm this because the somatic data of the study population were not reported in most series. Our results are in accord with those recently reported by Suma and colleagues for a population with a body structure similar to that of our patients [24].

Because IMA flow is in part destined to supply muscular tissue of the thoracic wall, vessel size and backflow could be determined by the degree of development of these muscular groups. In fact, in our study, the retrograde IMA flow correlated significantly only with variables related to body size. The latter also correlated significantly with the retrograde flow through the musculophrenic artery but not with that through the superior epigastric artery. In our experience, the retrograde flow through the musculophrenic artery constituted more than 70% of the overall retrograde IMA flow. Because there were no differences according to size or blood pressure in both terminal branches, the greater backflow in the musculophrenic artery probably resulted from its better collateralization with the descending thoracic aorta through the last intercostal arteries. In contrast, the superior epigastric branch connects with the ascending inferior epigastric artery through high-resistance terminal vessels. Preservation of the musculophrenic artery and as many intercostal branches as possible appears to be of great importance to achieve an adequate graft. Such was the technique used in previous clinical cases and experimental studies [2, 3, 14, 15], in which retrograde flow exceeded that which occurred in our experience. Although the retrograde IMA graft could be expected to be especially useful for patients with a large body frame and well-developed thoracic muscles, we failed to find a critical body size defining the group of patients with suitable retrograde IMA. No somatic variable showed a significant correlation with the antegrade IMA flow.

Diastolic and mean arterial pressure, which correlated significantly with the antegrade IMA flow, failed to correlate with the retrograde flow through the distal IMA and its terminal branches. This suggests the influence of unknown anatomical conditions, such as the development of collaterals or the presence of unreversed arterial spasm during the flow measurements. The first hypothesis is strongly supported by the significant increase in the reversed IMA flow found experimentally late after proximal IMA ligation [15]. On the other hand, the importance of arterial spasm, even when preventive measures are taken, was recently stressed by Mills and Bringaze [25]. Moreover, injection of papaverine into the short distal IMA end might result in a less beneficial effect than in the large proximal end owing to its "bleeding off" through adjacent collateral branches.

Pulse pressure delay between the antegrade and retrograde IMA was responsible for the modest but statistically significant increase in the diastolic flow/overall flow ratio (0.60 versus 0.57). The absolute value of the DFC of the retrograde IMA was significantly smaller than that of the antegrade IMA, however. This appears to result from the lower mean pressure in the former, a consequence of the high-resistance vessels that supply it. Coincidentally, the same ratio found in our study between DFC and overall flow in the retrograde IMA [0.60] was found by Folts and associates [15] when they compared the flow in the already anastomosed retrograde IMA to the previously measured free flow. Assuming that the ratio of Folts and associates [15] is constant, 40% of our patients would have an effective reversed IMA graft flow greater than 10% of the expected LVCF. Theoretically, this amount of flow corresponds to the expected flow of coronary vessels such as the posterior descending artery or posterolateral branches in most patients [6]. In fact, in 40% of our patients, the DFC in the retrograde IMA was greater than the EBF of at least one of such arteries. Because of the limited pressure and flow capacity of the retrograde IMA observed in our study, however, it appears reasonable to restrict its use to graft coronary vessels with high-grade stenosis or complete occlusion. There is no reason not to assume that the retrograde IMA has the same capacity of demand-responsive size adaptation as the proximally based antegrade IMA [9].

Although the main objective of maximizing the use of arterial grafts is to assure a durable and unimpeded myocardial blood supply, the possibility of a reoperation always exists, especially in younger patients. Reoperations in patients with retrograde IMA grafts could increase the difficulty of the procedure, mainly when the IMA is grafted to the left anterior descending artery, as is the case in other extraanatomical arterial grafts (ie, right gastroepiploic artery). Later abdominal operations might also pose risk to the retrograde IMA flow if the superior epigastric artery were damaged.

Based on our results, use of the retrograde IMA to revascularize coronary branches not suitable for the antegrade pedicled IMA in select patients appears reasonable. For this purpose, both terminal branches and as many intercostal arteries as possible should be preserved. The greater flow supply expected if the graft is so prepared should counteract the greater impedance of the longer pedicle necessary to use the retrograde IMA in the clinical setting. This would require further confirmation, however. Because retrograde flow magnitude cannot be fully anticipated, it should always be measured once the IMA is divided as high as possible; an insufficient retrograde flow would induce us to use the IMA as a free graft. This technique of revascularization could be especially useful in patients with a large body structure and in patients with obstruction or stenosis of the ipsilateral subclavian artery.

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Artificial Mitral Valve Chordae: Experimental and Clinical Experience

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Failure of mitral valve reconstructive procedures often may be ascribed to severe or progressive alterations of subvalvar apparatus. Expanded polytetrafluoroethylene sutures were used to replace anterior leaflet mitral valve chordae in 8 animals (hypertensive dogs and growing sheep). After the positive results obtained during a 13-month follow-up, 5-0 sutures of the same material were introduced in clinical practice to replace mitral valve chordae. Twelve patients had two to six anterior leaflet chordae replaced for degenerative or rheumatic disease. In 3 patients, the intraoperative result was not acceptable and a prosthetic valve was inserted during the same operation. One case of late failure has been recorded so far (18 months after the procedure), owing to rupture of a natural chorda shortened at operation. Since that event, we have implanted supportive artificial chordae in case of diffuse alteration of natural chordae. The remaining patients show satisfactory hemodynamic results, and no valve-related events have been recognized up to 30 months after operation. We suggest use of 5-0 polytetrafluoroethylene sutures in replacing anterior leaflet chordae in degenerative, rheumatic, and congenital mitral valve diseases.

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Mitral valve repair has obvious theoretical advantages over replacement with an artificial device. For successful repair, all the disordered components of the mitral apparatus must be fixed in each case. Annular dilatation is successfully handled by suture [1–4] or ring [5, 6] annuloplasty, but neglect of chordal elongation will result in a poor outcome [4]. Chordal elongation may be successfully treated with different shortening procedures [7, 8], and posterior leaflet chordal rupture is repaired with rectangular resection [7]. Multiple rupture of the anterior leaflet chordae still presents difficulty [6, 9, 10]. The posterior cusp transposition advocated by Carpentier [7, 11] presents limitations related to the degree of diffuseness of the disease: the posterior scallop that is to be transposed must be normal; if a normal scallop is transposed but the remaining posterior cusp is abnormal, the result may be unsatisfactory.

Both experimentally and clinically, pericardium from various sources and prepared in various ways has been extensively used for cusp and chordal replacement and repair [10, 12–16]. Pericardium prepared with glutaraldehyde behaves better in chordal applications than when it is used as cusp material. However, although it heals well to both cusp and papillary muscle and neither elongates nor shortens, it does thicken with time and would be of questionable utility for multiple chordal replacement. In the cardiothoracic surgery laboratory of the Albert Einstein College of Medicine, 2-0 and 3-0 expanded polytetrafluoroethylene (ePTFE) stitches (W.L. Gore & Assoc, Flagstaff, AZ) were introduced for chordal replacement in juvenile sheep with striking results [16]. The ePTFE sutures became covered with host tissue so that both histologically and grossly they resembled natural chordae. This observation was confirmed by Revuelta [17]. The combination of 2-0 ePTFE and tissue covering produced chordae that were less flexible than normal, however. In the hope of achieving new chordae with flexibility equivalent to normal chordae, we tested 5-0 ePTFE sutures for chordal replacement in juvenile sheep. We report these experimental studies and the results of introduction of this procedure to clinical use in the cardiac surgery department of Ospedale Regionale, Treviso, Italy.

Material and Methods

Animal Experiments

At Albert Einstein College of Medicine in 1985, we performed eight animal experiments: four in dogs (naturally hypertensive greyhounds) and four in weanling sheep. All animals received humane care in compliance with the "Guide for Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). The anesthetic management and the surgical procedure for establishing cardiopulmonary bypass have been reported previously [18]. In each animal, two to four first-order anterior leaflet chordae (ALC) were replaced by 5-0 ePTFE stitches. The sutures were attached to the papillary muscles in mattress shape and were reinforced with Teflon or PTFE pledgets, one on each side of the muscle, with two chordae obtained for each stitch. The two ends of the suture were fixed separately to the margin of the anterior leaflet, with the

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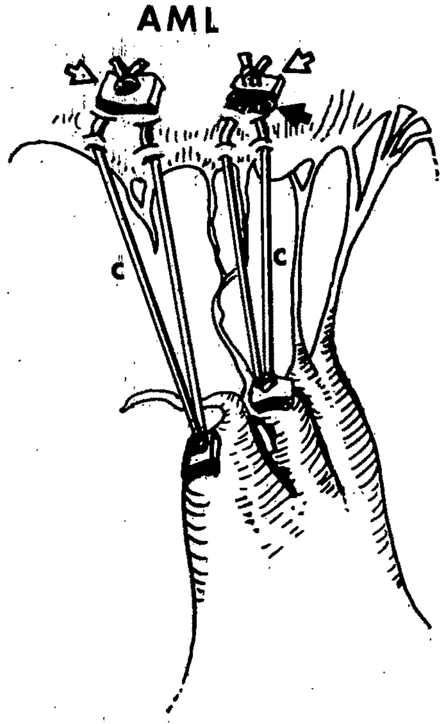


Fig 1. Expanded polytetrafluoroethylene suture (c) replacing two main chordae of the mitral valve anterior leaflet (AML). Open arrows *indicate PTFE pledgets.* Dark arrow *shows hemostatic clip.*

stitch brought through the edge and tied around a hemostatic clip (Edward Weck, Research Triangle Park, NC) or a small PTFE pledget (Fig 1). The exact length of the artificial chorda was set according to the rules suggested by Frater and colleagues [10–12].

After the animal was weaned from CPB, left atrial and left ventricular pressures were recorded. Cephalothin, 1 g, was administered subcutaneously for 5 days postoperatively. No anticoagulant regimen was instituted. One dog died of bleeding 24 hours after operation. The 7 surviving animals were followed for signs of mitral incompetence; only 1 showed such signs. The animals were killed electively 6 to 13 months after operation; before they were killed, we performed a cardiac catheterization with left ventriculography in 5 animals. After gross examination, the specimens were fixed for light microscopy and scanning electron microscopy.

Clinical Experience

After experimental results were obtained, we began clinical use of 5-0 ePTFE sutures in the treatment of mitral valve pathology in the Treviso (Italy) cardiac surgery department. From November 1986 to November 1988, 12 patients underwent open heart operation with implantation of two to six artificial chordae. Clinical data are shown in Table 1. The procedure was performed using cardiopulmonary bypass with moderate hypothermia (28°C) and crystalloid cardioplegic arrest. The technique of chordal insertion was identical to the experimental procedure except that after the two ends had been fixed at the proper length by the hemostatic clip (Edward Weck) the ends were passed through a small ePTFE pledget and tied. Suture [4] or Carpentier-Edwards ring (American Edwards Laboratories, Santa Ana, CA) annuloplasties were performed in 7 and 2 patients, respectively; other associated procedures are shown in Table 2. In no patient was chordal replacement the only procedure. The result was evaluated intraoperatively in all patients by left ventricle pressure filling with saline solution under direct vision and, after weaning from cardiopulmonary bypass, by epicardial two-dimensional echocardiography in the last 7 patients. No anticoagulant therapy was instituted. The follow-up has been obtained from all patients by direct examination, and the result is controlled by two-dimensional echocardiography every 6 months.

Table 1. Clinical Data

Patient No.	Sex	Age (y)	NYHA Class	Cause	Mitral Dysfunction	Chordae	Commissures	Leaflets	Prolapse	Associated Valvar Disease
1	F	65	IV	Deg.	Incomp.	Broken, elong.	. . .	Myx.	Ant.	. . .
2	M	34	II	Deg.	Incomp.	Broken, elong.	. . .	Myx.	Ant.	. . .
3	F	62	II	Rheum.	Incomp.	Broken, fused	. . .	Calcif.	. . .	. . .
4	M	41	III	Rheum.	Incomp.	Elong.	. . .	Calcif.	Ant.	AO, sten.
5	F	38	III	Rheum.	Sten.	Fused	Fused	Calcif.	. . .	. . .
6	F	55	II	Deg.	Incomp.	Broken, elong.	. . .	Myx.	Ant., post.	. . .
7	M	49	II	Deg.	Incomp.	Broken, elong.	. . .	Myx.	Ant., post.	. . .
8	F	40	III	Rheum.	Sten., incomp.	Elong.	Fused	Calcif.	Ant.	. . .
9	M	59	III	Deg.	Incomp.	Elong.	. . .	Myx.	Ant., post.	. . .
10	M	61	IV	Endoc.	Incomp.	Broken	. . .	. . .	Ant., post.	AO, tric. incomp.
11	F	57	III	Rheum.	Incomp.	Broken	. . .	. . .	Ant.	. . .
12	M	51	III	Rheum.	Sten., incomp.	Broken, fused	Fused	. . .	Ant., post.	. . .

Ant. = anterior; AO = aortic; calcif. = calcific; deg. = degenerative; elong. = elongated; endoc. = endocarditis; incomp. = incompetence; myx. = myxomatous; NYHA = New York Heart Association; post. = posterior; rheum. = rheumatic; sten. = stenosis; tric. = tricuspid.

Table 2. Surgical Procedures

					Intraoperative	
Patient No.	PTFE Chordae	Side	Associated Mitral Procedures	Associated Valvar Procedures	Hydrodynamic Test	Two-Dimensional Echocardiography
1	4	Ant.	Chordae shortening, suture annuloplasty	. . .	No incomp.	
2	2	Ant.	Suture annuloplasty	. . .	2+ incomp.[a]	
3	4	Ant.	CA debridement, suture annuloplasty	. . .	2+ incomp.[a]	
4	2	Ant.	Suture annuloplasty	AVR	No incomp.	
5	2	Ant.	Commissurotomy, CA debridement, suture annuloplasty	. . .	No incomp.	
6	6	Ant., post.	Suture annuloplasty	. . .	1+ incomp.	2+ incomp.[a]
7	4	Ant.	Rectangular resection, suture annuloplasty	. . .	No incomp.	No incomp.
8	4	Ant.	Commissurotomy, suture annuloplasty	. . .	No incomp.	No incomp.
9	4	Ant.	Rectangular resection, ring annuloplasty	. . .	No incomp.	No incomp.
10	2	Ant.	Suture annuloplasty	AVR, tric. annuloplasty	1+ incomp.	1+ incomp.
11	2	Ant.	Ring annuloplasty	. . .	No incomp.	No incomp.
12	2	Ant.	Rectangular resection, ring annuloplasty	. . .	No incomp.	No incomp.

[a] Mitral valve replaced during the same operation.

AVR = aortic valve replacement; CA = calcium; PTFE = polytetrafluoroethylene; other abbreviations as in Table 1.

Results

Animal Experiments

Cardiac catheterization performed before the animals were killed showed only 1 case of mild mitral incompetence, which was demonstrated, at gross examination, to result from an incorrect chordal measurement at operation. Gross examination showed all artificial chordae to have retained their original length. In 1 animal, the two ends of the same suture were placed too close, became fused, and formed one chorda with, however, a diameter still similar to that of natural chordae (Figs 2, 3). The healing to the papillary muscle was good in all instances, whereas on the cusp side 2 animals had a mild inflammatory reaction. The pliability was gravity-tested in the fresh specimens, comparing the degree of bending of the explanted host incorporated artificial chordae and the same length of natural chordae in response to gravity; they were identical [19].

At histological examination, the sutures appeared to be progressively covered, from both papillary muscle and leaflet sides, by a uniform sheath of fibrous tissue (Fig 4) connected with the underlying artificial tissue by fibrous bridges. The surface was smooth and almost completely covered by a neointimal cellular sheath (Fig 5). Our observations confirmed previous data [16] from our laboratory suggesting that the fibrous tissue overgrowth is a self-limiting process; no significant differences could be found in the thickness of the sheath among animals investigated from 6 to 13 months after operation. No calcification or thrombi were detected. No differences in gross and histological findings were noted between sheep and hypertensive dogs.

Clinical Experience

INDICATIONS. Tables 1 and 2 show that clinical application of the technique of chordal replacement as an adjunct to the many other maneuvers of mitral valve repair has rapidly resulted in extension of the indication beyond the simple presence of a ruptured anterior cusp chorda.

Calcium debridement was the cause for chordal replacement in 2 patients (see Table 2); in these patients, after we performed a commissurotomy, the leaflet motion was still restricted owing to calcification of major chordae up to the leaflet junction, while the pliability of the nonappositional part of the leaflet was satisfactory. The calcified chordae were therefore replaced by two ePTFE sutures. Four other patients had four to six artificial chordae inserted as support of diffusely diseased subvalvar apparatus (elongation and weakening of most first-order chordae, besides the rupture of at least one of them).

INTRAOPERATIVE RESULTS. With the hydrodynamic intraoperative test, the result was judged to be satisfactory in 10 patients, whereas 2 patients (1 with rheumatic and the other with degenerative mitral disease) had the valve replaced.

FOLLOW-UP RESULTS. No hospital mortality was registered among the 12 patients, and the 9 who were discharged

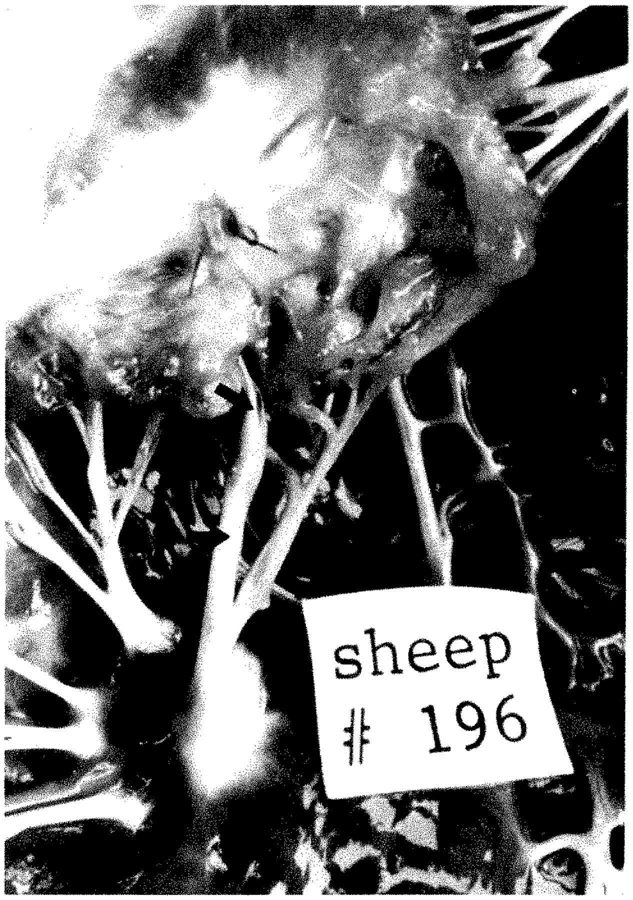


Fig 2. Experimental specimen in which two artificial chordae, although fused in one sheath (arrows), *retained a diameter similar to natural chordae.*

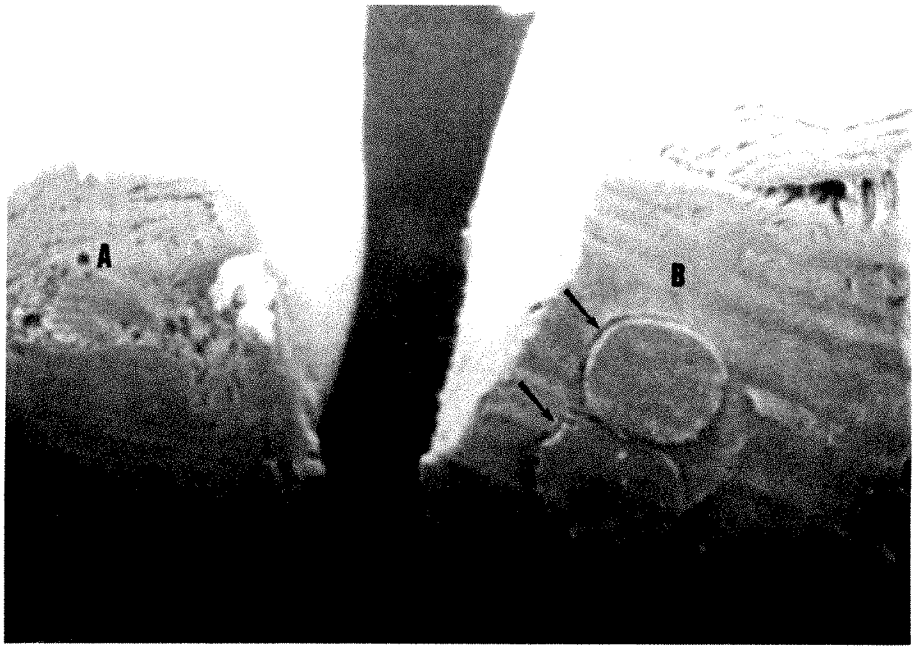
from the hospital with artificial chordae have been followed by two-dimensional echocardiography (Table 3). So far only 1 patient (the 1 in whom chordae shortening had been performed) showed recurrence of mitral regurgitation 18 months after operation. The sudden manifestation of clinical signs of mitral incompetence indicated urgent operation. At reoperation, one of the shortened natural chordae was torn and the suture annuloplasty dehisced, while the artificial chordae were still in proper position with retained length. Gross and histological examinations showed changes similar to those of the experimental specimens with a slower rate of host tissue overgrowth (Fig 6). Since that experience, in patients with diffuse myxomatous chordal and leaflet degeneration we have inserted new chordae in the presence of attenuated as well as ruptured native chordae and have used a ring for the annuloplasty.

No deaths or other valve-related complications have been recorded, and the patients are in functional class I (7 patients) or II (1 patient) after a follow-up ranging from 2 to 25 months (mean, 12.3 months).

Comment

After the disappointing results obtained with the triangular resection of the anterior mitral leaflet, two valuable techniques have been suggested for correcting ALC multiple rupture [7, 11]: fixing the leaflet free edge to secondary chordae and transposition of posterior leaflet cusp and chordae. In both cases, almost normal strong chordae, adjacent or opposite to the damaged area, are required to obtain a satisfactory result; such chordae are not present in most degenerated valves. Moreover, the potential for progression of the disease of residual abnormal chordae

Fig 3. Same specimen as in Figure 2 observed by scanning electron microscopy. Natural chordae (A) *and artificial chordae* (B) *show the two fused expanded polytetrafluoroethylene sutures* (arrows). *(×35 before 29% reduction.)*



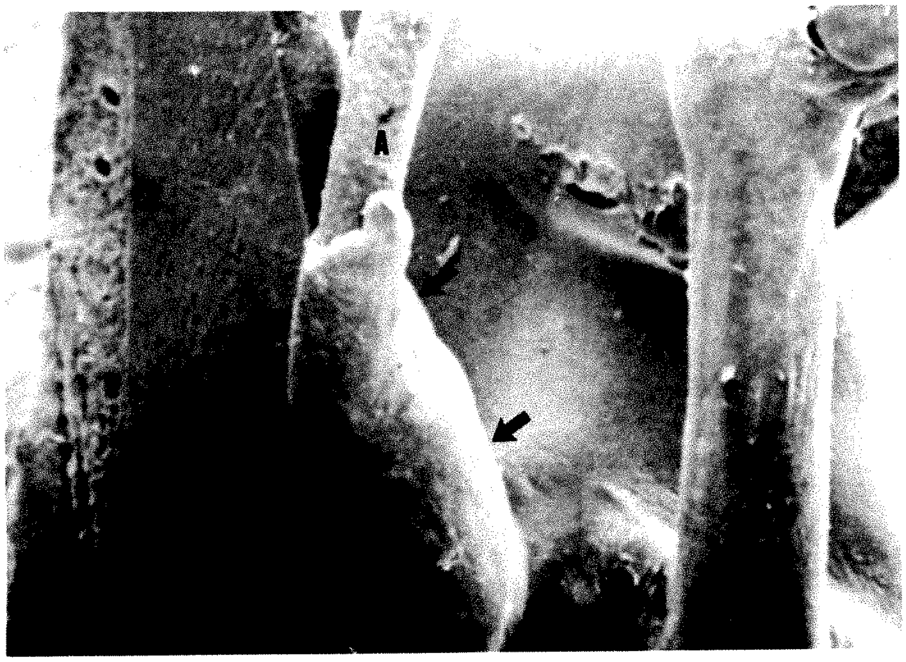


*Fig 4. Expanded polytetrafluoroethylene chordae (*A*) partially covered by growing fibrous tissue (*arrows*). (×25 before 29% reduction.)*

has always been a concern. In the past, these factors caused multiple ALC rupture to be a contraindication to mitral valve repair [4, 6, 9]. Postrheumatic calcification of ALC often results in restricted motion of the anterior leaflet even after a proper commissurotomy with papillary muscle splitting [4]; only replacement of the calcified chordae would restore an adequate valve motion in these cases. The tendency of biological materials used for this purpose to stiffen [10, 12–15] led us to be cautious about their use in this application.

For these considerations we began a program to evaluate the feasibility of replacing ALC with artificial chordae. The new ePTFE was chosen for the theoretical advantages connected with the microstructure of this material with its property of permitting attachment and infiltration of collagen cells and potential neointimal growth [16]. Vetter and co-workers [16] showed, however, that 2-0 and 3-0 sutures covered by a neofibrosa and neointima became thicker than natural chordae. Our experiments with 5-0 ePTFE sutures completely confirmed the previous findings with thicker sutures but yielded new chordae as flexible as the native chordae. With further independent experimental confirmation from Revuelta [17], we proceeded to clinical trials. At first, indications were limited

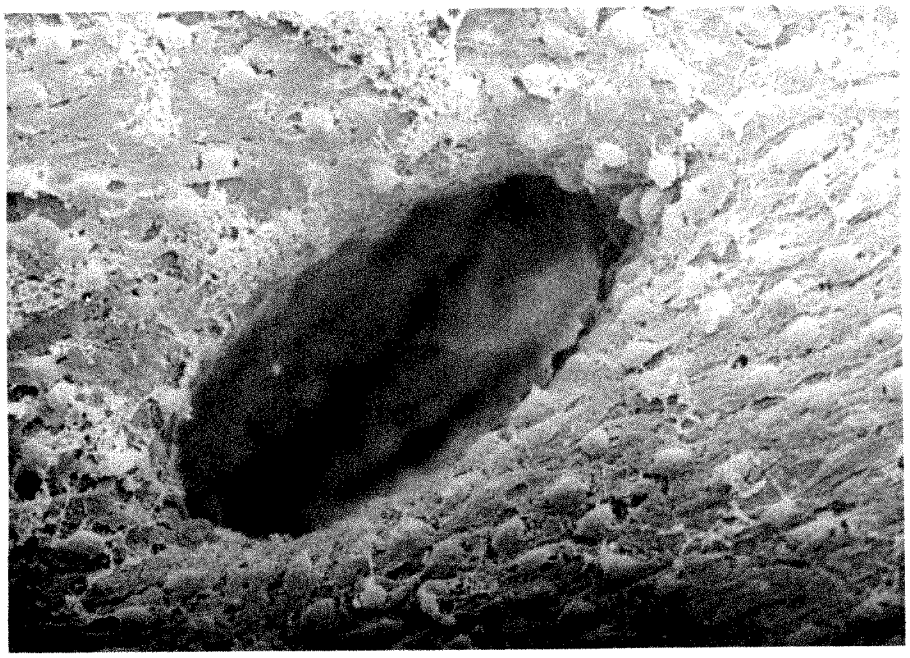


*Fig 5. The sheet of neoendothelial cells covering the fibrous tissue is incomplete, resulting in a portion of exposed expanded polytetrafluoroethylene sutures (*A*).*

Table 3. Follow-up

Patient No.	Months	NYHA Class	Two-Dimensional Echocardiography (6 mo)	Valvar Area (cm²)	MVR
1	18	III	No incomp.	2.8	Yes[a]
4	25	I	No incomp.	2.2	No
5	20	I	No incomp.	2.5	No
7	15	I	No incomp.	3.0	No
8	15	I	No incomp.	2.6	No
9	7	I	No incomp.	3.0	No
10	6	II	Mild incomp.	2.8	No
11	3	I	. . .	. . .	No
12	2	I	. . .	. . .	No

[a] Eighteen months after operation owing to recurrent mitral regurgitation.

Incomp. = incompetence; MVR = mitral valve replacement; NYHA = New York Heart Association.

to young patients with degenerative pathology and multiple rupture of ALC. The preliminary reassuring findings in these cases, and the report of similar clinical results by David [20], led us to extend the application to rheumatic disease as well when the stiffness of some chordae maintained a restricted motion of the anterior leaflet after commissurotomy. Finally, the only postoperative failure in our series, which resulted from progression of degenerative disease, indicated a further application as support in patients with diffuse myxomatous chordal alterations.

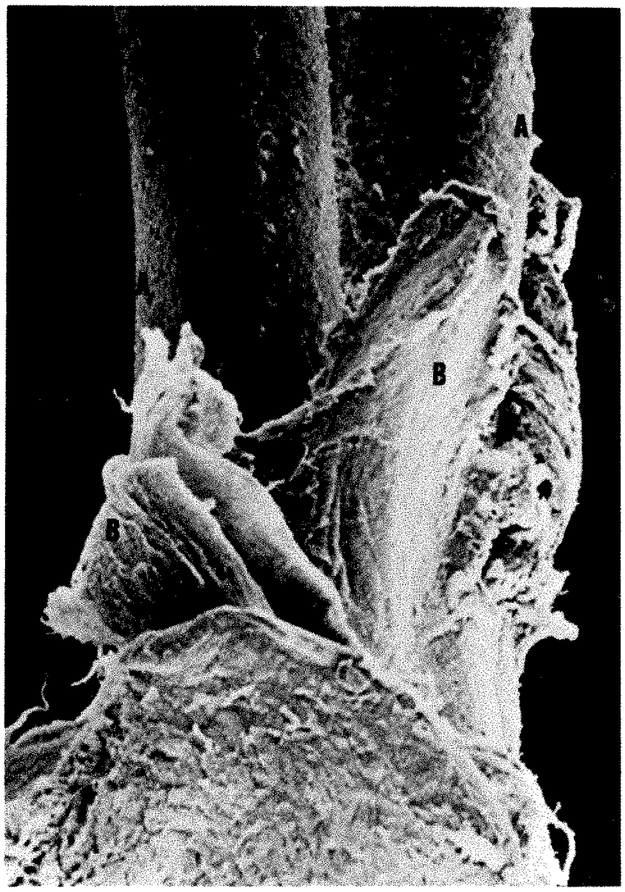


Fig 6. Clinical specimen from the only reoperated patient (see text for explanation). The artificial chordae (A) are still almost completely uncovered by fibrous tissue (B), demonstrating a slower rate of tissue overgrowth in comparison with experimental specimens.

The relative ease of this technique does not result in excessive ischemic time and allows the possibility of prompt valve replacement without excessive risk. The conventional limits in mitral valve reconstruction can be pushed without increasing operative risk [21].

In our experience the intraoperative assessment of mitral valve function, performed by hydrodynamic tests and two-dimensional echocardiography, was shown to be reliable in predicting postoperative results. So far, we have observed no failure of the artificial chordae in clinical use up to 30 months of follow-up.

The early clinical experience using ePTFE as chordal replacement in rheumatic and degenerative mitral valve disease has been encouraging. Its use as an adjunct to the other maneuvers of mitral valve repair has made it possible to retain valves that otherwise would have needed replacement.

The laboratory investigation could not have been done without the technical skills of A. Leon, P. Bon, F. Rivera, and F. Wasserman.

During the laboratory investigation, Dr C. Zussa was Research Fellow of the W. R. Heart Foundation at Albert Einstein College of Medicine, Bronx, New York.

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Notice From the Southern Thoracic Surgical Association

The Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Cerromar Beach, Puerto Rico, November 8–10, 1990. There will be a $155 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 8, 1990. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Advance registration forms, hotel reservation cards, and details regarding transportation arrangements will be mailed to Association members. Nonmembers should write to the Secretary-Treasurer, Gordon F. Murray, MD.

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Effects of Left Ventricular Assist for Cardiogenic Shock on Cardiac Function and Organ Blood Flow Distribution

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Organ blood flow distribution was studied in dogs subjected to a left ventricular assist device (LVAD). In normal hearts (group 1), left ventricular work was reduced by 25% when 35% of cardiac output was performed by the LVAD. Organ perfusion, measured with tracer microspheres, remained normal or slightly increased. After induction of cardiogenic shock (group 2), perfusion deteriorated in all organs, but first in the brain, kidney, and intestinum. All animals died within 1 hour. When maximal inotropic support was administered after shock (group 3), hemodynamics improved but perfusion to most organs decreased progressively and 83% of animals died within 2 hours. When the LVAD was inserted after shock but without inotropic support (group 4), perfusion of all organs became normal during LVAD except for kidney flow, which remained severely depressed (56% of preshock value). After LVAD insertion, hemodynamics did not recover completely, and 33% of the animals died within 3 hours. When use of the LVAD was combined with 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine after shock (group 5), organ blood flow distribution became normal during and after LVAD use except for renal flow, which was significantly impaired (83% of preshock value). Hemodynamics recovered after LVAD use, and all animals survived in this group. We conclude that use of the LVAD combined with low-dose positive inotropic support can prevent deterioration of organ perfusion after cardiogenic shock except for kidney.

(Ann Thorac Surg 1990;50:374–83)

Since Stuckey and colleagues [1] applied a mechanical circulatory assist system for a patient in 1957, many new systems have been developed [2, 3]. The basic idea of a left ventricular assist device (LVAD) is very simple: the blood entering the left atrium and the left ventricle, which cannot be pumped out by the failing heart, is removed through a cannula and, by means of an extracorporeal pump, is driven into the arterial system [3, 4]. It is possible to reach high flows during support using this technique. The LVAD does not use an oxygenator, and full heparinization is not necessary. It can be implanted for several hours up to several days and can be removed when the heart is able to sustain its own circulation. The decision to implant such a device is difficult for many reasons, however. First, use of an LVAD implies chronic implantation of cannulas connected to an extracorporeal pump system. Furthermore, removal of the system requires a second operation. Both factors increase the risk of postoperative infection considerably. Second, how fast and to what extent the failing myocardium will recover is generally unknown. Third, because implantation of an LVAD is always preceded by a certain period of cardiogenic shock, organ blood flow (brain, kidney, liver) is compromised and the extent to which the LVAD system is able to restore organ flow distribution is not clear. Organ flow distribution is very difficult to study in humans. Therefore, we developed a model of cardiogenic shock in experimental animals that is very close to the clinical condition. We evaluated cardiac function, coronary circulation, and blood flow distribution in all organs during shock and after LVAD support.

Material and Methods

Models and Surgical Procedure

This study was performed in 29 mongrel dogs of either sex and unknown age, weighing 25 to 31 kg. Anesthesia was performed with 0.1 mL/kg Hypnorm (fluanizon, 10 mg; fentanyl, 0.2 mg/mL) intramuscularly and intravenous injection of 0.25 mg/kg sodium pentobarbital (Nembutal) and 0.1 mg/kg pancuronium bromidum (Pavulon). The dogs were intubated and ventilated with 60% oxygen + 40% air (Mark-7 BIRD). After anesthesia, a median sternotomy was performed, and the heart was suspended in a pericardial cradle. A pulmonary artery thermodilution catheter (9F, American Edwards Laboratory) was introduced into the pulmonary artery through the outflow tract of the right ventricular wall. A small catheter (2.5F, Edslab injectate catheter) was placed into the right atrial appendage for injection of cold Ringer's solution. Another catheter (8F) was introduced into the ascending aorta through the right axillar artery for measurement of aortic pressure (fluid-filled system). A Millar-type tip manometer (Gaeltec-Dimed) was introduced into the left ventricle

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through the apex. A small polyvinyl chloride catheter was placed into the left atrium for the injection of tracer microspheres. Both femoral arteries were dissected free for the arterial inflow (12 USCI aortic cannula) of the cardiopulmonary bypass (CPB) (according to the protocol). Through the right femoral vein, a polyvinyl chloride catheter (6F) was introduced into the inferior vena cava for the infusion of volume and drugs. According to the protocol, a single venous drainage cannula (36F, Sarns) was introduced into the right atrium for installation of CPB.

MODEL OF CARDIOGENIC SHOCK. After heparinization (200 U/kg Heparin Nova), cardiogenic shock was produced by intermittent occlusion of the left coronary artery at 37°C while the animal was placed on CPB. The CPB system was primed with 800 mL of Ringer's lactate (Normosol-R), 20 mL of sodium bicarbonate, 10 mL of 20% mannitol, and 500 U of heparin. During CPB, mean arterial pressure was kept at about 50 mm Hg and minimum perfusion flow was maintained at 80 $mL \cdot kg^{-1} \cdot min^{-1}$. The left anterior descending branch (LAD) and left circumflex branch (LCX) were occluded for 20 minutes, followed by reperfusion for 5 minutes. The ischemic period of 20 minutes was repeated twice. After ischemia, the dogs were weaned from CPB and hemodynamics were measured. Additional ischemic periods were then induced (10 minutes each) during intermittent periods of CPB until the desired low cardiac output (CO) level was reached. In the dog, the left coronary artery supplies the entire left ventricle, so that right ventricular function remains intact. This is important because only under this condition will oxygenation be maintained in the presence of an assisted left circulation. The total duration of left ventricular ischemia was chosen so that a significant reduction in CO was obtained after discontinuation of CPB. A reduction of 50% from control CO was considered cardiogenic shock.

LEFT VENTRICULAR ASSIST SYSTEM. A large, flexible cannula (36F, Sarns) was introduced in the left atrium through the left appendage and exteriorized through the chest wall and connected to a Bio-Medicus magnet-driven pump system. Such a system has important advantages over a roller-pump system in terms of avoiding hemolysis during long-term perfusion [5]. The circuit was primed with Ringer's lactate.

HEMODYNAMIC MEASUREMENTS. The hemodynamic measurements were continuously monitored during control conditions, during cardiogenic shock, and during and after LVAD support. Electrocardiogram (ECG) was recorded on a Hewlett-Packard multichannel device. Heart rate (HR) was calculated from the monitored ECG. Aorta and pulmonary artery pressure were measured with PDCR-75 transducers (Druk Limited). Left ventricular pressure (LVP) and its first derivative (LVdP/dt) were measured using a catheter-tip micromanometer. These pressures were recorded continuously. Cardiac output was measured at regular time intervals using the thermodilution technique by connection to a Hewlett-Packard 15055 CO computer. Stroke volume (SV), left ventricular stroke work index (LVSWI), left cardiac work (LCW), right cardiac work (RCW), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) were calculated by the following equations: SV (mL/beat) = CO/HR; LCW = CO × (mAoP − LVEDP) × 0.0136; RCW = CO × (mPAP − CVP) × 0.0136; LVSWI (g · m/kg) = SV/BW × (mAoP − LVEDP) × 0.0136; SVR = (mAoP − CVP)/CO; PVR = (mPAP − LVEDP)/CO; where BW = body weight, mAoP = mean aortic pressure, mPAP = mean pulmonary artery pressure, LVEDP = left ventricular end-diastolic pressure, and CVP = central venous pressure.

ORGAN BLOOD DISTRIBUTION. Organ flow distribution was measured using tracer microspheres. Four differently labeled types of microspheres (15 μm diameter) were used (^{141}Ce, ^{95}Nb, ^{103}Ru, and ^{113}Sn). Absolute flow values were obtained by calibration with the "artificial organ technique" [6]. The tracer microspheres were injected into the left atrium. After termination of the experiment, the organs of interest were removed and representative samples were taken, weighed, and coded. These organs were brain (left and right hemisphere, cerebellum); heart (left and right ventricle); liver; kidneys; intestine (duodenum); pancreas; muscle (temporal muscle); and skin (abdomen). The organ samples were transferred to plastic vials, and radioactivity was counted with a Nuclear Data gamma counter and an automatic sample changer.

Biochemical Analysis

Blood samples were drawn from the right atrium at regular intervals for determination of the level of plasma hemoglobin, creatinine, and electrolytes. Blood gas samples were taken from the arterial catheter and right atrium catheter, and these were analyzed for pH, oxygen tension, CO_2, carbon dioxide tension, base excess, and hemoglobin with ABL-2 acid-base laboratory blood gas analyzer (Radiometer). Alveolar-arterial O_2 difference (A-aDO_2) and pulmonary shunt (Qs/Qt) were calculated by the following equations: $A - aDO_2 = PAo_2 - PaO_2$; $Qs/Qt = [0.0031 \times p(A - aDO_2)]/[0.0031 \times p(A - aDO_2) + c(a - vDO_2)]$, where PAo_2 = alveolar partial pressure of oxygen, PaO_2 = arterial partial pressure of oxygen, and $a - vDO_2$ = arterial venous oxygen difference. Urine output was collected during the experiment.

Experimental Protocol

The animals were divided into five groups.

GROUP 1 (N = 6): NORMAL DOGS, 1 HOUR OF LEFT VENTRICULAR ASSIST DEVICE. In group 1, the effect of 1 hour of LVAD on general hemodynamics and organ flow distribution was studied. In a condition not preceded by cardiogenic shock, tracer microspheres were injected before and at the end of 1 hour of LVAD use.

GROUP 2 (N = 5): CARDIOGENIC SHOCK, NO SUPPORT. In group 2, the effect of cardiogenic shock on general hemodynamics and organ flow distribution was studied. Out-

Table 1. Influence of Left Ventricular Assist Device on Hemodynamics in Normal Dogs[a]

	Minutes After LVAD			
Variable	Control	30	60	60
HR (beats/min)[b]	119 ± 32	146 ± 33	145 ± 37	164 ± 42
mAoP (mm Hg)	79.1 ± 17.0	77.8 ± 10.3	75.8 ± 11.4	66.5 ± 12.9
CO (L/min)[b]	2.8 ± 0.8	3.3 ± 0.8	3.2 ± 0.8	3.0 ± 0.8
SV (mL/beat)[c]	24.2 ± 7.1	16.5 ± 8.6	16.3 ± 8.2	19.4 ± 9.2
mPAP (mm Hg)	15.3 ± 3.8	16.0 ± 5.3	17.1 ± 3.3	18.8 ± 2.1
LVEDP (mm Hg)	6.4 ± 1.7	6.4 ± 1.7	7.2 ± 1.8	7.2 ± 3.0
CVP (cm H_2O)	4.4 ± 1.7	6.2 ± 3.9	5.8 ± 3.6	7.0 ± 4.0
LVSWI (m · g/kg)[b]	1.00 ± 0.41	0.67 ± 0.43	0.65 ± 0.41	0.67 ± 0.41
LVdP/dt_{max} (mm Hg/s)	2,492 ± 517	2,068 ± 791	2,282 ± 1,114	2,498 ± 1,145
LVdP/dt_{min} (mm Hg/s)	1,709 ± 579	1,664 ± 342	1,805 ± 475	1,528 ± 519
LCW (m · g)	2.72 ± 0.76	2.17 ± 0.81	2.06 ± 0.81	2.46 ± 1.01
RCW (m · g)	0.43 ± 0.09	0.52 ± 0.27	0.55 ± 0.19	0.56 ± 0.24

[a] Data are shown as mean ± standard deviation. [b] $p < 0.05$ and [c] $p < 0.01$, significant influence of LVAD (repeated measures analysis of variance).

CO = cardiac output; CVP = central venous pressure; HR = heart rate; LVAD, left ventricular assist device; LCW = left cardiac work; LVdP/dt_{max}, LVdP/dt_{min} = maximal or minimal rate of change of left ventricular pressure; LVEDP = left ventricular end-diastolic pressure; mAoP = mean aortic pressure; mPAP = mean pulmonary artery pressure; RCW = right cardiac work; SV = stroke volume.

come in terms of survival for 2 hours after induction of cardiac failure was used to assess the severity of the model. Tracer microspheres were injected before and after induction of cardiac failure.

GROUP 3 (N = 6): CARDIOGENIC SHOCK WITH MAXIMAL POSITIVE INOTROPIC SUPPORT (20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ DOPAMINE). After induction of cardiac failure, an infusion of dopamine was started, hemodynamics were measured, and organ flow distribution was studied early (at 5 minutes) and late (1 hour) during positive inotropic support.

GROUP 4 (N = 6): CARDIOGENIC SHOCK WITH LEFT VENTRICULAR ASSIST DEVICE SUPPORT. Immediately after induction of cardiac failure, the LVAD was started and continued for 1 hour. To reach a successful degree of left ventricular assist, the following criteria were used: Bio-Medicus pump flow rate of 50% of the preshock CO and a left ventricular filling pressure of at least 5 to 10 mm Hg. Organ flow distribution was assessed under control conditions, at the end of LVAD use, and 1 hour after the LVAD was stopped. No positive inotropic support was added during the LVAD support.

GROUP 5 (N = 6): CARDIOGENIC SHOCK, LEFT VENTRICULAR ASSIST DEVICE SUPPORT COMBINED WITH LOW-DOSE POSITIVE INOTROPIC SUPPORT. The same protocol was followed as for animals of group 4, but an infusion of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine was started together with the LVAD procedure and continued during the post-LVAD period. The same measurements were performed as in group 4.

Statistical Analysis

The results obtained were expressed as mean values ± standard deviation (Tables 1–7) or ± standard error of the mean (Figs 1–5).

Repeated measures analysis of variance was used for evaluating changes over time when there were adequate numbers of serial measurements in each subject (group 1: Table 1). If data characteristics precluded repeated measures analysis, *t* tests were used to compare the between-group values of the difference between the individual time points and baseline values. Therefore, all preshock baseline values (hemodynamic data: Figs 1 and 2) were pooled and compared with group values at individual time points. A p value less than 0.05 was considered significant. Differences in mortalities between the groups were tested using the χ^2 test.

Results

Effects of Left Ventricular Assist Device on Hemodynamics and Organ Blood Flow in Normal Hearts (Group 1)

General hemodynamics were measured before, during, and after 60 minutes of LVAD use. The results are shown in Table 1. During LVAD use, at a flow rate of 1 L/min, CO increased significantly (approximately 14%); left ventricular contractility (dP/dt_{max}) and LVSWI decreased significantly. Aortic pressure and pulmonary artery pressure remained unchanged. Left ventricular end-diastolic pressure and CVP were maintained in the same range by intravenous infusion of fluid. Left cardiac work decreased by 20%, and RCW increased by 10%.

Organ blood flow distribution was measured before and at 60 minutes of LVAD support. The results are shown in Table 2. The increase in total CO did not result in a homogeneous increase in flow to all organs. In some organs, perfusion decreased slightly but not significantly ($p > 0.05$) (muscle and pancreas flow). In others, the mean flow increased, although moderately and not statistically significantly ($p > 0.05$) (duodenum, liver, and kidney). Brain, left and right ventricular myocardium, and skin,

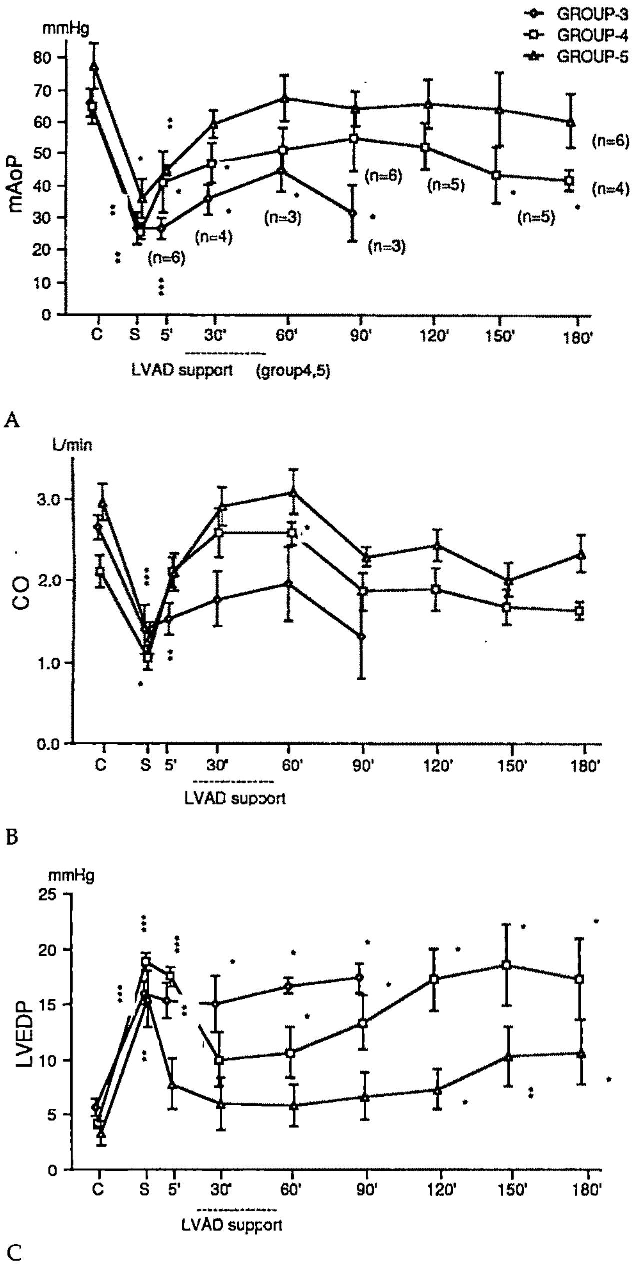

Fig 1. Influence of left ventricular assist device (LVAD) and/or positive inotropic support on hemodynamics after cardiogenic shock. Groups 4 and 5 were supported for 60 minutes by LVAD. Values are shown as mean ± standard error of the mean. (C = control; CO = cardiac output; LVEDP = left ventricular end-diastolic pressure; mAoP = mean aortic pressure; S = cardiogenic shock; * *p* < 0.05, ** *p* < 0.01, *and* *** *p* < 0.001 *versus baseline.)*

however, showed significant increase in flow during LVAD support. The increase ranged between 1.7 times control in skin to 3.6 times control in the right ventricle.

Effects of Cardiogenic Shock on Hemodynamics and Organ Blood Flow (Group 2)

In 5 dogs cardiogenic shock was produced by intermittent occlusion of the LAD and the LCX during CPB. The average ischemic time was 48.0 ± 7.6 minutes (Table 3).

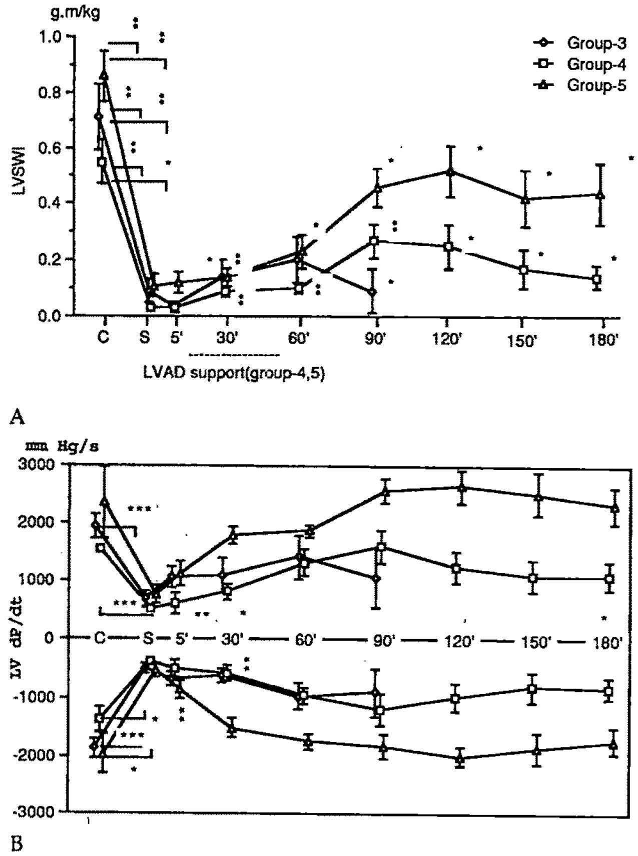

Fig 2. Influence of left ventricular assist device (LVAD) and/or positive inotropic support on hemodynamics after cardiogenic shock. Groups 4 and 5 were supported for 60 minutes by LVAD. Values are shown as mean ± standard error of the mean. (C = control; LV dP/dt = first derivative of left ventricular pressure; LVSWI = left ventricular stroke work index; S = cardiogenic shock; * *p* < 0.05, ** *p* < 0.01, *and* *** *p* < 0.001 *versus baseline.)*

Table 2. Influence of Left Ventricular Assist Device on Organ Flow Distribution in Normal Dogs[a]

Organ	Control	LVAD (60 min)
Brain	25.2 ± 8.6	61.3 ± 21.3[b]
Cerebellum	23.9 ± 6.5	52.3 ± 17.1[b]
Duodenum	62.6 ± 13.7	71.5 ± 45.7
Pancreas	31.4 ± 4.9	29.3 ± 24.3
Liver	12.2 ± 7.5	31.6 ± 23.2
Muscle	5.3 ± 6.5	4.6 ± 1.8
Skin	3.1 ± 2.2	5.4 ± 2.4[b]
Right ventricle	51.1 ± 21.5	151.9 ± 56.2[c]
Left ventricle	80.5 ± 40.5	167.3 ± 56.6[c]
Endocardial/epicardial ratio	1.24 ± 0.19	1.03 ± 0.51
Kidney	264.5 ± 81.0	312.1 ± 188.6

[a] Organ blood flow data are expressed in milliliters per minute per 100 g. Values are shown as mean ± standard deviation. [b] $p < 0.05$ and [c] $p < 0.01$ versus control (paired Student's t test).

LVAD = left ventricular assist device.

Table 3. Clinical Outcome

Group	Ischemia Time (min)	Mortality 180 min After Cardiogenic Shock (%)
2 (nonsupport)	48 ± 8	100
3 (inotropic support)	51 ± 14	83
4 (LVAD)	48 ± 16	33[a]
5 (LVAD + inotropic support)	52 ± 11	0[a,b]

[a] $p < 0.01$ versus group 2 by χ^2. [b] $p < 0.05$ versus group 3 by χ^2.

LVAD = left ventricular assist device.

After the animals were weaned from CPB, hemodynamics deteriorated significantly. None of the animals received any inotropic or mechanical support. Five minutes after the dogs were weaned from CPB, all hemodynamics were changed. The results are shown in Table 4. Cardiac output decreased to 54% of the preischemic value ($p < 0.05$) and HR decreased to 82% of the preischemic value ($p < 0.05$). All animals died within 60 minutes (range, 5 to 60 minutes) after being weaned from CPB (see Table 3).

Organ blood flow distribution was measured at 5 minutes after termination of CPB. In 2 animals, ventricular fibrillation developed shortly before the tracer microsphere could be injected so that blood flow measurements were obtained in only 3 animals. The results are shown in Table 5. Flow decreased dramatically in most organs. Brain flow decreased to 29%, kidney flow decreased to 26%, and intestinal flow decreased to 18% of control ($p < 0.05$). Pancreas and muscle flow changed inconsistently.

Effects of Positive Inotropic Support on Hemodynamics and Organ Blood Flow Distribution During Cardiogenic Shock (Group 3)

In six dogs, cardiogenic shock was induced as in group 2. Ischemic time was about the same as in the previous group (50 ± 14 min) (see Table 3). Five minutes after termination of CPB but before the start of dopamine infusion, hemodynamic variables did not differ significantly from those in group 2. Mean aortic pressure, CO, $LVdP/dt_{max}$ and $LVdP/dt_{min}$, SV, and LVSWI were significantly decreased ($p < 0.05$ or less) as compared with the preischemic condition; LVEDP and CVP were significantly increased ($p < 0.05$).

Table 4. Influence of Cardiogenic Shock on Hemodynamics 10 Minutes After Weaning from Cardiopulmonary Bypass

Variable	Control	Cardiogenic Shock
HR (beats/min)	143 ± 24	115 ± 12[b]
mAoP (mm Hg)	95.5 ± 31.7	42.0 ± 19.7[c]
CO (L/min)	2.1 ± 0.1	1.2 ± 0.3[b]
SV (mL/beat)	15.4 ± 3.4	10.7 ± 4.0[c]

[a] Values are shown as mean ± standard deviation. [b] $p < 0.05$ and [c] $p < 0.01$ versus control (paired Student's t test).

Abbreviations are as in Table 1.

Table 5. Influence of Cardiogenic Shock on Organ Blood Flow Distribution[a]

Organ	Control	Cardiogenic Shock
Brain	23.1 ± 0.3	6.7 ± 9.4[b]
Cerebellum	19.3 ± 0.9	6.0 ± 9.4[b]
Duodenum	43.9 ± 11.5	8.1 ± 2.9[b]
Pancreas	18.8 ± 4.8	29.6 ± 11.8
Liver	7.7 ± 4.8	4.0 ± 2.9
Muscle	2.7 ± 0.6	4.8 ± 2.7
Skin	1.0 ± 0.2	0.3 ± 0.4
Right ventricle	47.6 ± 40.3	18.6 ± 10.6
Left ventricle	66.4 ± 58.4	26.3 ± 11.1
Endocardial/epicardial ratio	1.21 ± 0.19	0.41 ± 0.20[b]
Kidney	202.3 ± 25.7	52.8 ± 28.3[b]

[a] Organ blood flow data are expressed in milliliters per minute per 100 g. Values are shown as mean ± standard deviation. [b] $p < 0.05$ versus control (paired Student's t test).

Five minutes after the start of the dopamine infusion, ($20\ \mu g \cdot kg^{-1} \cdot min^{-1}$) all hemodynamic variables remained unchanged ($p > 0.05$) as compared with the shock state. In group 3, the first 2 animals died at 30 minutes after cessation of CPB. At that time mAoP, CO, $LVdP/dt_{min}$, SV, and LVSWI remained significantly lower ($p < 0.05$) than the control values in the surviving 4 animals; LVEDP and CVP remained elevated ($p < 0.05$). After 60 minutes, another animal died, and after 90 minutes 2 more animals died. Hemodynamic data of the surviving animals at the different observation periods are shown in Figures 1 and 2.

During dopamine infusion, organ blood flow was measured at 5 minutes in all dogs and at 60 minutes in the 3 surviving animals. Brain flow and myocardial flow (left and right ventricle) remained unchanged during this period (Fig 3). Perfusion of the kidney, however, decreased to 33% of control at 5 minutes and to 40% of control at 60 minutes ($p < 0.05$). Flow to the intestine, pancreas, and muscle also decreased significantly as compared with the control situation ($p < 0.05$). Flow to the liver and skin remained unchanged.

Effects of Left Ventricular Assist Device Support on Recovery of Hemodynamics and Organ Blood Flow Distribution After Cardiogenic Shock (Group 4)

In 6 dogs, cardiogenic shock was produced as described. The average ischemic time was 48 ± 16 minutes (see Table 3). Cardiogenic shock induced effects on hemodynamics comparable with those in groups 2 and 3 in terms of changes in CO, mAoP, $LVdP/dt_{max}$ and $LVdP/dt_{min}$, LVEDP, CVP, and LVSWI ($p > 0.05$). Heart rate, however, was higher and SV was lower in group 4 than in group 2 during the shock state ($p < 0.05$). The results of group 4 are summarized in Figures 1 and 2.

Five minutes after induction of cardiogenic shock, the animals were placed on the LVAD for 1 hour. During this period, mAoP, CO, $LVdP/dt_{max}$ and $LVdP/dt_{min}$ in-

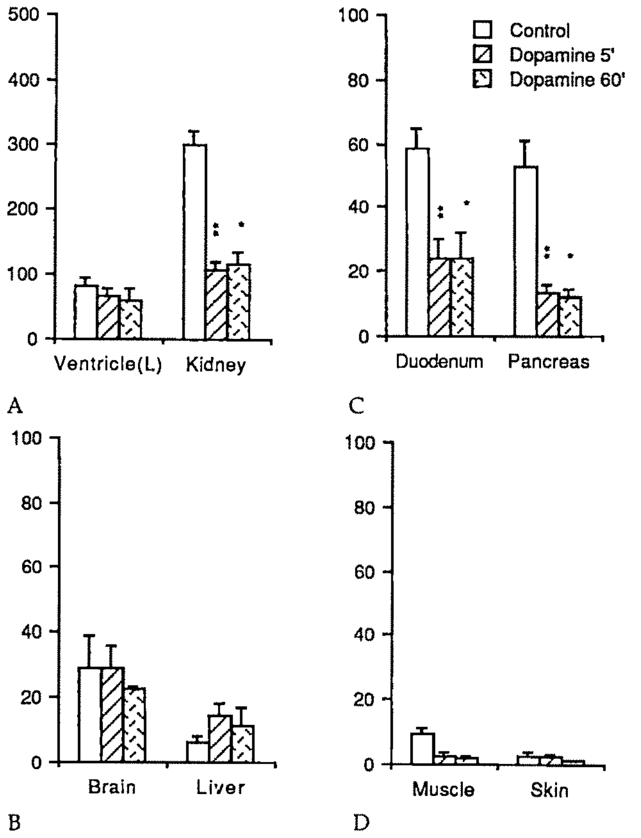

Fig 3. Influence of positive inotropic support on organ blood flow (milliliters per minute per 100 g) distribution after cardiogenic shock (group 3). Values are shown as mean ± standard error of the mean. (p < 0.05 and ** p < 0.01 versus control [paired Student's t test].)*

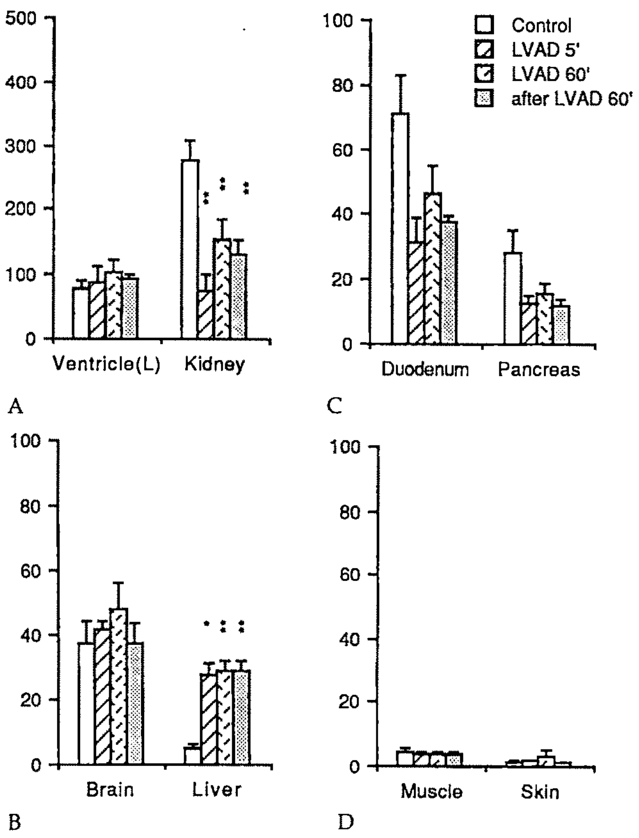

Fig 4. Influence of left ventricular assist device (LVAD) on organ blood flow (milliliters per minute per 100 g) distribution after cardiogenic shock (group 4). Values are mean ± standard error of the mean. (p < 0.05 and ** p < 0.01 versus control [paired Student's t test].)*

creased significantly ($p < 0.05$). Left ventricular end-diastolic pressure decreased significantly ($p < 0.05$).

After 1 hour of support, the LVAD was stopped and hemodynamics were followed for the next 120 minutes. Within 60 minutes after termination of LVAD 1 animal had irreversible cardiac failure and died (see Table 3). Ninety minutes after termination of LVAD, another animal died. Four of the 6 animals completed the protocol. During the first 30 minutes, mAoP, CO, and LVdP/dt$_{max}$ remained significantly higher than the corresponding values during the shock state ($p < 0.05$). Left ventricular end-diastolic pressure increased, however, as compared with the LVAD phase and was not significantly different from that during the shock state.

Organ blood flow distribution in group 4 was measured under control conditions, at 5 and 60 minutes of LVAD support, and at 1 hour after weaning from LVAD. One hour after termination of LVAD support, 5 of 6 animals were still alive, so that organ flow distribution could be measured at this interval. Because only 4 of 6 animals were alive 2 hours after termination of LVAD support, no further flow measurements were calculated.

During the 1 hour of LVAD support, brain, cerebellum, duodenum, pancreas, muscle, skin, and myocardial flow were not significantly changed as compared with the control state ($p > 0.05$) (see Fig 4).

Hepatic flow also increased during LVAD support in group 4, but kidney flow remained decreased (see Fig 4; Table 6). The surviving 5 dogs had exactly the same flow distribution 1 hour after weaning from LVAD as during

Table 6. Changes in Organ Blood Flow

Organ	Group 2, Cardiogenic Shock	Group 4, Shock + LVAD After LVAD	Group 5, Shock + LVAD + Dopamine After LVAD
Brain	–	=	=
Cerebellum	–	=	=
Duodenum	–	=	=
Pancreas	=	=	=
Liver	=	+	+
Muscle	=	=	=
Skin	=	=	=
RV	=	=	+
LV	=	=	+
Kidney	–	–	–

Symbols: blood flow increased (+); blood flow decreased (–); blood flow unaltered (=).

LVAD = left ventricular assist device; LV = left ventricle; RV = right ventricle.

the LVAD phase (see Fig 4; Table 6). Most organ flows tended to decrease after LVAD use was stopped, however. As shown in Figure 4, brain flow was never jeopardized during or after LVAD support, but duodenum and pancreas flow showed a strong, although not significant, tendency to decrease.

Effects of Left Ventricular Assist Device Support Combined With Low-Dose Dopamine on Recovery of Hemodynamics and Organ Blood Flow Distribution After Cardiogenic Shock (Group 5)

In 6 dogs, cardiogenic shock was produced as described. The average ischemic time was 52 ± 11 minutes (see Table 3). Cardiogenic shock induced effects on hemodynamics comparable with those induced in groups 2, 3 and 4, except for HR, which was significantly higher than in group 2 ($p < 0.05$). The results are summarized in Figures 1 and 2. Five minutes after induction of cardiogenic shock, the animals were placed on LVAD support for 1 hour; low-dose dopamine (5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was also added. During the LVAD phase, aortic pressure, CO, and $LVdP/dt_{max}$ and $LVdP/dt_{min}$ increased significantly ($p < 0.05$) as compared with the shock state. Pulmonary artery pressure and LVEDP decreased significantly ($p < 0.05$) (see Figs 1, 2). At the end of the LVAD phase, none of the hemodynamic variables were significantly different from those during the control state ($p > 0.05$). After weaning from LVAD, none of the animals died (see Table 3). During the post-LVAD phase, hemodynamics remained relatively stable. Mean aortic pressure, CO, SV, and $LVdP/dt_{min}$ were slightly lower than during the control phase but not significantly different ($p > 0.05$); $LVdP/dt_{max}$ was slightly above the control level. Mean pulmonary artery pressure showed a tendency to increase, and LVEDP and CVP were significantly higher than during the control phase ($p < 0.05$) and LVSWI was significantly lower than during the control phase ($p < 0.05$).

Organ blood flow distribution in group 5 was measured during control, at 5 and 60 minutes of LVAD plus dopamine support, and at 60 minutes after the dogs were weaned from LVAD. During LVAD plus dopamine support, organ flow distribution was not significantly different from the preischemic phase ($p > 0.05$) except for the hepatic flow, which was increased ($p < 0.05$). Flow to the brain and the cerebellum was slightly higher than in control, although not significant ($p > 0.05$). Flow to the duodenum, pancreas, and kidney was lower than during control but the differences were not statistically significant ($p > 0.05$). Myocardial flow increased significantly ($p < 0.05$) in the early LVAD plus dopamine period. The results are summarized in Figure 5.

After the dogs were weaned from LVAD but during the low-dose dopamine infusion, organ blood flow distribution was approximately the same as during LVAD + dopamine. Brain flow remained in the normal range, but duodenum and pancreas flow decreased slightly more. The differences as compared with the control values remained not significant, however ($p > 0.05$). Myocardial flow increased further as compared with the control state ($p < 0.05$). Kidney flow, however, decreased to 53% of the preshock value ($p < 0.05$). The results of organ blood flows measured in all the experimental series are summarized in Table 6.

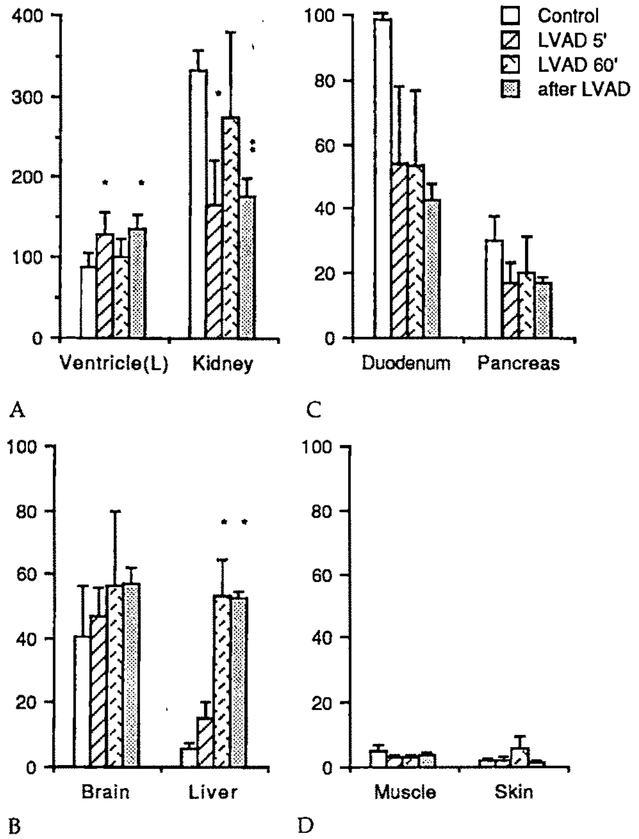

Fig 5. Influence of left ventricular assist device (LVAD) plus low-dose positive inotropic support on organ blood flow (mL · min^{-1} · 100 g^{-1}) distribution after cardiogenic shock (group 5). Values are mean ± standard error of the mean. ($p < 0.05$ and ** $p < 0.01$ versus control [paired Student's t test].)*

Effects of Left Ventricular Assist Device on Respiratory Function Under the Open Chest Condition

In 3 additional control dogs, respiratory function was followed for 2 hours under open chest conditions without LVAD (not given in the protocol). Next, in dogs placed on LVAD support under nonischemic conditions (group 1), respiratory function was determined during the 60 minutes of LVAD support and 60 minutes after the dogs were weaned from the LVAD.

In the experiments without LVAD, all variables remained unchanged. In group 1 (open chest with LVAD), PaO_2 decreased and $A\text{-}aDO_2$ increased significantly ($p < 0.05$). Pulmonary shunt (Qs/Qt) also increased but was not statistically significant. Results are shown in Table 7.

Comment

Experimental Model of Cardiogenic Shock

In an experimental approach to studying left ventricular assist systems, one of the most important factors is the

Table 7. Influence of Open Chest and Left Ventricular Assist Device on Respiratory Function

Variable	LVAD	Control	60 min
PaO$_2$ (mm Hg)	Without	375 ± 211	416 ± 191
	With	380 ± 108	250 ± 160[a]
PaCO$_2$ (mm Hg)	Without	20.1 ± 3.1	18.6 ± 5.1
	With	21.7 ± 2.6	23.8 ± 4.2
A-aDO$_2$ (mm Hg)	Without	354 ± 212	313 ± 195
	With	347 ± 107	474 ± 157[a]
Qs/Qt (%)	Without	1.2 ± 0.1	1.5 ± 0.2
	With	1.8 ± 2.2	5.1 ± 9.2

[a] $p < 0.05$ versus control (paired Student's t test).

A-aDO$_2$ = alveolar-arterial O$_2$ difference; LVAD = left ventricular assist device; PaCO$_2$ = arterial partial pressure of CO$_2$; PaO$_2$ = arterial partial pressure of oxygen; Qs/Qt = physiological pulmonary shunt ratio.

choice of a good model to produce cardiac failure in a standardized way comparable with that of the clinical setting. Cross-clamping of the aorta [7], selective ligation of a coronary artery [8], or intracoronary injection of particles are commonly used to produce cardiac failure. These techniques, however, have considerable disadvantages. Cross-clamping of the aorta produces global biventricular failure and is therefore unsuitable for LVAD experiments [8].

Embolization of the myocardium with particles can certainly induce myocardial damage, but biochemical or functional recovery of the damaged myocardium does not occur during or after support because of the irreversible nature of such a coronary obstruction. The problem in selective ligation in dog coronary arteries is that many variations exist in the size of the perfusion area and in the degree of preexisting collateral flow; therefore, it is difficult to produce comparable degrees of cardiac failure in different animals [9].

In our experimental setting, cardiac failure was produced by intermittent occlusion of the left coronary arteries at 37°C while the dogs were placed on CPB. After a constant period of ischemia, the dogs were weaned from CPB and hemodynamics were measured. Additional periods of ischemia were induced after resumption of CPB until postischemic CO deteriorated to 50% of its preischemic control value. In this way, we were able to create a selective and standardized left ventricular failure.

The average time necessary to produce a satisfactory level of cardiogenic shock was 50 minutes. During this shock state, blood flow in all organs was decreased. When no pharmacological or mechanical support was offered during cardiogenic shock (group 2), all animals died within 60 minutes after weaning from CPB. This shows the severity of the model. We believe that this shock model can be applied to study effects of LVAD in terms of preservation of organ blood flow distribution, recovery of cardiac function, and clinical outcome.

Effects of Left Ventricular Assist Device on Hemodynamics and Organ Blood Flow Under Nonischemic Conditions

Rose and co-workers [10] studied the effect of the LVAD on the normal heart in dogs. During LVAD support, CO increased by 11% and mAoP and LVdP/dt$_{max}$ were slightly decreased. Fukuda and colleagues [11] showed that LVdP/dt was decreased after a significant increase in flow of the LVAD system, but the decrease in contractility was not significant. In our experiments, total CO increased by 14% when the LVAD pumped 30% of the original CO. This small increment in total CO resulted from an imbalance between the LVAD pump rate and the additional filling of the circulatory bed because we tried to maintain LVEDP and CVP constant. Left cardiac work diminished by about 25%, which means a significant reduction in myocardial oxygen consumption. The small increase in total CO, however, resulted in a 10% increase in right cardiac work. After termination of LVAD, hemodynamics did not return to control conditions completely because we increased filling of the circulatory system. This was evidenced by the increase in CVP, LVEDP, PAP, CO, and RCW (although not significantly). The decreased LVSWI originated from a relative tachycardia as compared with the control state. This tachycardia might result from manipulation of the heart.

During LVAD support, myocardial blood flow increased to two times control values for the left ventricle ($p < 0.05$). Intramyocardial flow distribution (endocardial/epicardial flow ratio) changed from 1.24 to 1.03; this change, however, was not statistically significant. This change is due to a slight decrease in subendocardial flow, which is considered to be the effect of nonpulsatile flow produced by the centrifugal pump. Axelrod and co-workers [12] reported that venoarterial bypass in dogs decreased the endocardial/epicardial ratio blood flow from 1.09 to 1.01 by nonpulsatile flow, and increased it from 1.09 to 1.38 by pulsatile flow.

Kidney blood flow may be strongly affected by a mechanical circulation system [13]. During extracorporeal circulation, despite maintenance of perfusion flow and blood pressure, renal blood flow decreases and renal vascular resistance increases [13]. In our experiments, renal blood flow was slightly increased, although not significantly. This suggests that the LVAD at least does not impair kidney flow under normal conditions.

Respiratory function, on the other hand, was clearly influenced by the LVAD: PaO$_2$ decreased and A-aDO$_2$ increased significantly. In a control series of experiments on open-chest, anesthesized animals without the LVAD, we did not observe any significant changes in respiratory function, which shows that the open-chest condition itself does not induce these changes and that most probably they are related to the LVAD system. Indeed, mechanical circulatory assist causes bleeding around the bronchial arteries, tissue edema, atelectasis [14], and collapse of the pulmonary veins owing to drainage from the left atrium by the LVAD system [15].

We conclude that assisting the left ventricle in the normal dog heart results in excessive flow when filling pressure is maintained. Respiratory function, however, appears to be very vulnerable in the presence of a LVAD system, and more investigations are necessary in this respect.

Effects of Positive Inotropic Support After Acute Cardiogenic Shock

Prolonged myocardial ischemia during cardiac operations decreases myocardial function in the postoperative phase. When this occurs, medical treatment is attempted to wean the patient from CPB. Detrimental effects of positive inotropic support have been reported, however [16], and this treatment has severe limitations when cardiac dysfunction is severe [17].

In our experiments, maximal inotropic support as the only treatment after induction of cardiogenic shock (group 3: 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine) resulted in a very high mortality at the end of the experiments. Furthermore, hemodynamic recovery in the surviving dogs was poor and the data did not differ from those of the shock state. Most organ blood flow values decreased during the dopamine support period. These results show that, in our model, positive inotropic support is insufficient in the treatment of severe cardiac failure.

Effects of the Left Ventricular Assist Device Itself and of the Left Ventricular Assist Device Combined With Low-Dose Inotropic Support After Cardiogenic Shock

Many investigators have described the indications, techniques, and driving conditions for LVAD [18]. Some report that restricted drainage from the left atrium is a limitation for the effect on left ventricular decompression and high flow support [19]. The optimal flow rate of the LVAD, however, is still unknown.

Namiki and associates [20] studied the influence of LVAD flow rate on coronary sinus and renal and carotid artery blood flow. They showed that the LVAD could improve hemodynamics after induction of cardiac failure, and that coronary sinus and renal and carotid artery blood flow remained unchanged provided the pump flow rate was more than 40%. Other investigators [21] reported that the LVAD flow also has a negative influence on the right ventricular function: maximum LVAD flow caused right ventricular dysfunction.

We believe that the combination of LVAD and low-dose inotropic support compensates for the disadvantage of left atrial drainage and makes the LVAD appropriate to restore cardiac function after cardiac failure. Whether driving a failing heart with inotropes can "exhaust" myocardial energy reserve and delay recovery is not known, however.

The true indication for use of the LVAD, however, is myocardial stunning, and this type of postischemic failure is not a problem of energy production but of energy utilization [17]. The stunned myocardium is stimulated by pharmacological interventions that increase cytosolic calcium [22]; therefore, we use a low-dose of the inotrope dopamine. When the myocardium is truly stunned, it will react to such a low dose and the exhaustive effect of high doses of cathecholamines can be avoided.

During 60 minutes of LVAD support after cardiogenic shock, blood flow to the myocardium remains unchanged. Uretzky and co-workers [23] reported a change of the endocardial/epicardial blood flow ratio in the ischemic myocardium after 3 hours of LAD occlusion: it decreased to 0.52 when the heart was supported by CPB and to 0.36 in the nonsupported group. In our experiments, this ratio decreased significantly from 1.21 to 0.41 in the nonsupport group and remained unchanged in the groups supported by an LVAD system, which shows that LVAD support maintains coronary blood flow and intramyocardial blood flow distribution during cardiac failure after ischemia.

The most common cause of death in patients on LVAD support is multiple organ failure, despite maintenance of hemodynamic variables. Abnormal flow to kidneys and liver may be the reason for multiorgan failure, and it is most unfortunate that LVAD support does not normalize these flows completely once they have deteriorated during severe shock conditions.

Under conditions of postischemic cardiac failure, renal blood flow remained significantly lower than in control conditions (56% of control) when the heart was supported only by the LVAD system. When LVAD was combined with low-dose positive inotropic support, however, renal blood flow recovered to about normal values (83% of control, $p > 0.05$). The influence of mechanical circulation on renal function is problematic, and many aspects are still unknown. During extracorporeal circulation, possible restrictive factors that influence renal blood flow are constriction of the renal arteries, acidosis, the presence of pulsatile or nonpulsatile flow, and blood pressure. As shown in many studies, LVAD use or CPB resulted in a decrease in renal blood flow despite maintenance of perfusion and blood pressure. On the other hand, in experiments in which cardiogenic shock was not used renal blood flow increased when the animals were placed on LVAD, and in long-term experiments with total artificial heart or LVAD systems renal function remained unchanged [24]. These experiments, however, were performed in normal animals.

We consider cardiogenic shock one of the most important determinants of renal failure. Only LVAD support combined with low-dose inotropic support is effective in maintaining renal blood flow. Hepatic artery flow was significantly increased to more than five times control flows during LVAD support. Concomitantly, intestinal and pancreas blood flow, which reflect portal vein flow, decreased. In experiments with the total artificial heart or ventricular assist devices, high portal vein pressure and pathological changes in the tissue surrounding the hepatic artery were noted [25]. These changes suggest that the LVAD induces abnormal intrahepatic blood flow distribution between hepatic artery and portal vein [25]. Such changes are attributed to abnormal hemodynamics on the arterial side. We consider high hepatic artery flow to be one of the causes of liver failure during left ventricular support. We conclude that LVAD combined with low-dose inotropic support is most effective in restoring myocardial function and organ blood flow after acute cardiogenic shock.

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Pharmacological Response of Internal Mammary Artery and Gastroepiploic Artery

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Pharmacological response of coronary artery bypass conduit is of great importance. This study was designed to clarify the contractile properties of internal mammary artery and gastroepiploic artery obtained from coronary revascularization. The response to ergonovine, serotonin, and phenylephrine was examined by isometric contraction recording apparatus. The concentration–response relation of both internal mammary artery and gastroepiploic artery to ergonovine, serotonin, and phenylephrine showed similar sigmoid curves. There were no significant differences in developed tension between internal mammary artery and gastroepiploic artery at any concentration for any agent. There were no significant differences in the 50% effective dose value for any agent between internal mammary artery and gastroepiploic artery. Internal mammary artery and gastroepiploic artery are reported to be similar in terms of size, flow capacity, and freedom from atherosclerosis. This study shows their equivalence from a pharmacological viewpoint.

(Ann Thorac Surg 1990;50:384–6)

The superiority of the long-term results of internal mammary artery (IMA) grafting as compared with those of saphenous vein (SV) grafting is now a matter of record [1, 2] and has led to dramatic expanded use of the IMA [3]. Gastroepiploic artery (GEA) grafting has also become popular because of its similarity to the IMA in terms of diameter, wall thickness, and freedom from atherosclerosis [4–6]. The pathophysiology of vascular tone regulation of these arterial conduits remains uncertain, however. This study was designed to clarify the contractile properties of the IMA and GEA in response to ergonovine, serotonin, and phenylephrine.

Material and Methods

Human IMA and GEA were obtained during operation from 24 patients receiving coronary artery bypass grafting (CABG). None of them were receiving adrenergic, muscarinic, or histaminic drugs during this study. The specimens were cleaned of surrounding tissues and cut into helical strips (width, 2 mm; length, 20 mm). Attention and care were given to maintaining and not disrupting the integrity of the endothelium.

The strips were placed in 30-mL organ baths containing buffer solution of the following composition (millimoles per liter): NaCl, 118; KCl, 4.0; $CaCl_2$, 1.5; $MgSO_4$, 1.2; NaH_2PO_4, 1.2; $NaHCO_3$, 25; and glucose, 5; they were then equilibrated with 95% O_2 and 5% CO_2 at 37°C. The segment was attached to a force-displacement transducer. Approximately 1.5 g of resting tension was applied to each segment by adding 20 mmol/L KCl. Previous laboratory studies have determined that this is the optimum tension for obtaining a maximal contractile response to the agonists studied. Recordings were made on a multichannel physiological recorder with light-sensitive paper. All drugs were added to the bath in a cumulative fashion; concentration–response relations were then generated. The following drugs were used: ergonovine maleate (ergonovine), 5-hydroxytryptamine creatinine sulfate (serotonin), and *l*-phenylephrine hydrochloride (phenylephrine).

Developed tensions were expressed as percentile contraction of resting tension to minimize the individual variations. The 50% effective dose (ED_{50}) value was defined as the concentration of drug at which 50% of the maximum response was obtained. It was calculated by probit analysis to compare sensitivity. Results were expressed as mean value ± standard error of the mean, and *t* tests were performed for statistical analysis.

Results

The concentration–response relations for ergonovine are shown in Figure 1. The recordings of both IMA and GEA showed similar sigmoid curves in response to ergonovine. There were no significant differences in percentile contraction between IMA and GEA at any concentration.

The concentration–response relations for serotonin are shown in Figure 2. The recordings of both IMA and GEA showed similar sigmoid curves in response to serotonin. There were no significant differences in percentile contraction between IMA and GEA at any concentration.

The concentration–response relations for phenylephrine are shown in Figure 3. The recordings of both IMA and GEA showed similar sigmoid curves in response to

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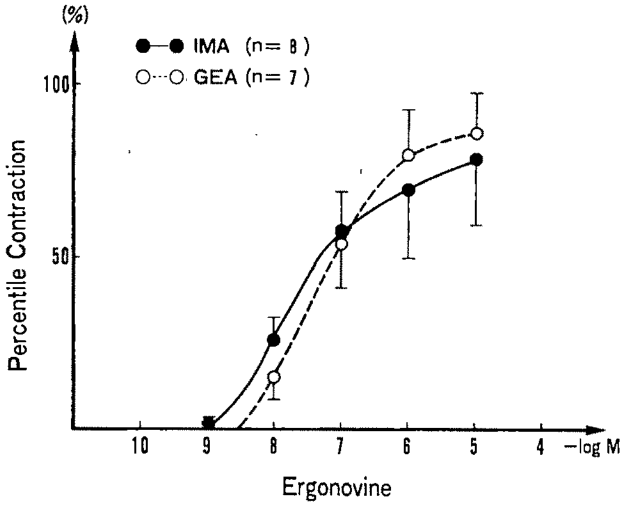

Fig 1. Concentration–response relations for ergonovine.

phenylephrine. There were no significant differences in percentile contraction between IMA and GEA at any concentration.

Maximum contractions for ergonovine were 78% ± 18% of IMA and 86% ± 14% of GEA, those for serotonin were 101% ± 16% of IMA and 106% ± 10% of GEA, and those for phenylephrine were 163% ± 18% and 179% ± 13%, respectively.

The ED_{50} value for ergonovine, serotonin, and phenylephrine is shown in Table 1. There were no significant differences between IMA and GEA for the three agents. The results suggest that the responses of both IMA and GEA to ergonovine, serotonin, and phenylephrine are entirely similar.

Comment

Spasm of large coronary arteries appears to play an important role in eliciting myocardial ischemia [7]. Recently, spasm of the coronary bypass conduit was reported [8]. Sarabu and colleagues [9] reported IMA graft spasm. Mills and Everson [6] described GEA graft spasm. To clarify the contractile properties of these coronary artery bypass conduits is of great importance.

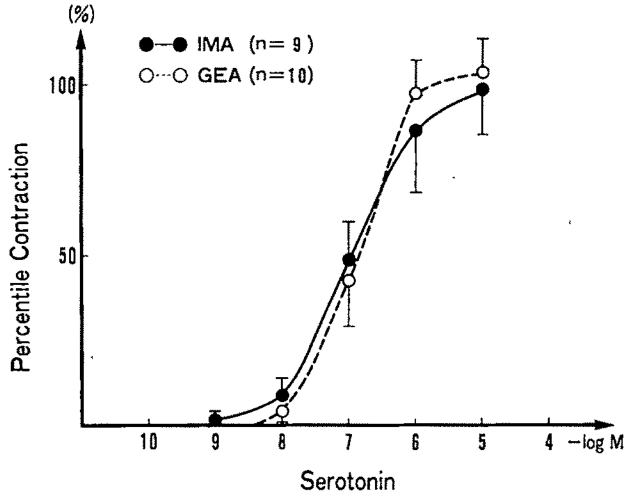

Fig 2. Concentration–response relations for serotonin.

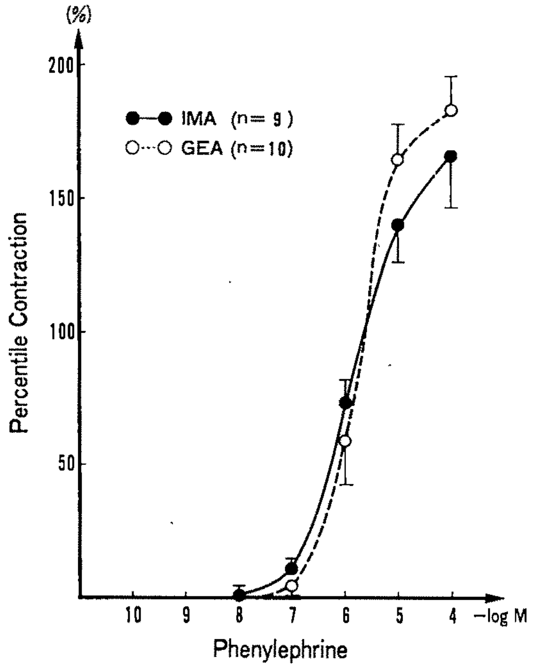

Fig 3. Concentration–response relations for phenylephrine.

Several pharmacological agents are used diagnostically to provoke native coronary artery spasm. Ergonovine is widely accepted as a specific and potent agent for this purpose [10]. Ergonovine has complex pharmacological properties with potential actions at serotonergic as well as α-adrenergic receptors [11]. Therefore, ergonovine, serotonin, and phenylephrine were used in this study.

The variability of vascular contraction noted among different vessels in the same individual is noteworthy. Ginsburg and associates [12], in a study of quantitative aspects of human coronary artery contraction in isolated epicardial coronary ring segments, reported that human coronary artery reacted more highly to serotonin than to phenylephrine and ergonovine. Our results showing that maximum contraction for phenylephrine of IMA and GEA were about two times higher than those for ergonovine

Table 1. The 50% Effective Dose for Ergonovine, Serotonin, and Phenylephrine in Internal Mammary Artery and Gastroepiploic Artery

Agent	IMA (mol/L)	GEA (mol/L)	Statistical Analysis
Ergonovine	$5.1 \pm 1.2 \times 10^{-8}$	$1.2 \pm 0.5 \times 10^{-7}$	NS
Serotonin	$1.1 \pm 0.3 \times 10^{-7}$	$2.0 \pm 0.4 \times 10^{-7}$	NS
Phenylephrine	$1.6 \pm 0.5 \times 10^{-6}$	$2.2 \pm 0.4 \times 10^{-6}$	NS

GEA = gastroepiploic artery; IMA = internal mammary artery; NS = not significant.

and serotonin allow us to speculate that these arterial conduits are more susceptible to α-adrenergic stimulation than to ergonovine or serotonin administration. Kitamura and colleagues [13] examined the dynamic responses of coronary arteries and IMA to pharmacological intervention in 5 patients with vasospastic angina. Based on postoperative angiography, they reported that the IMA graft was unresponsive to ergonovine, at least in the amount required to produce coronary artery spasm. They also reported that the IMA graft appears to function well in patients with vasospastic angina. Our results showing that pharmacological responses of IMA and GEA are similar suggest that GEA as well as IMA will be a conduit of choice for bypassing not only coronary arteries with fixed stenoses but also coronary arteries that develop spasm in variant angina.

According to our clinical experience [14, 15], IMA and GEA are approximately the same size. Both arteries in situ are straight vessels with little tortuosity, and they have few branches. In addition, they are reported to be similar in terms of diameter, wall thickness, free flow and freedom from atherosclerosis [4–6]. This study has shown that IMA and GEA are also equivalent from a pharmacological viewpoint.

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Complement Activation With Bubble and Membrane Oxygenators in Aortocoronary Bypass Grafting

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Thirty-three patients admitted for coronary bypass grafting were randomized to cardiopulmonary bypass with a bubble oxygenator (Cobe or Polystan) or a membrane oxygenator (SciMed). Plasma concentrations of C3 activation products and the terminal complement complex were measured using enzyme immunoassays. Both variables increased almost linearly after onset of cardiopulmonary bypass, with maximal concentrations at closure of the sternum. From a baseline of 7.5 to 12.0 arbitrary units (AU)/mL (medians), the concentrations of C3 activation products increased by 117.5 AU/mL (Cobe), 120.5 AU/mL (Polystan), and 213.3 AU/mL (SciMed). The increase in the membrane group was significantly higher than in the two bubble oxygenator groups ($p < 0.01$). From a baseline of 0.9 to 1.3 AU/mL, the concentrations of terminal complement complex increased by 5.4 AU/mL (Cobe), 6.6 AU/mL (Polystan), and 7.7 AU/mL (SciMed) (differences not significant). The higher C3 activation caused by the membrane oxygenator may be explained by differences in flow profile and surface area in contact with blood. The study cannot confirm the general assumption that membrane oxygenators lead to lower complement activation than do bubble oxygenators.

(Ann Thorac Surg 1990;50:387–91)

Complement activation during cardiopulmonary bypass (CPB) is correlated to postoperative cardiac, renal, and pulmonary dysfunction [1], abnormal bleeding [1], and increased requirement for mechanical ventilation [2]. Heparin–protamine complexes and factors related to the oxygenator appear to be main activators of complement during CPB [3, 4]. Efforts have therefore been made to develop oxygenators with a low tendency to activate complement. Even so, the concentrations of various activation products formed during CPB are substantial [5, 6]. Membrane oxygenators in general have been claimed to cause less complement activation than bubblers owing to reduced blood–air interface. We compared complement activation with use of one membrane and two bubble oxygenators in patients undergoing aortocoronary bypass grafting.

Material and Methods

Patients and Procedures

Thirty-three patients, 29 men and 4 women, admitted for routine coronary bypass grafting were included after giving informed consent. Inclusion criteria were left ventricular ejection fraction greater than or equal to 0.40, absence of major noncardiac illness, normal liver function, and no history of recent steroid use. The patients were randomly assigned to CPB with one of the following oxygenators: the hard-shell bubbler Cobe Optiflo II (Cobe Laboratories, Lakewood, CO) (n = 11), the collapsible bubbler Polystan VT-11500 (Polystan, Copenhagen, Denmark) (n = 10), and the nonporous silicone-membrane SciMed I-3500 oxygenator (SciMed Life Systems, Minneapolis, MI) (n = 12). A Swank HF-6000 arterial line filter (Pioneer Viggo, Beaverton, OR) and a Gambro roller pump (Gambro, Horten, Norway) were used for all operations. The extracorporeal circuit was primed with a standard mixture of 500 mL dextran 70 (60 mg/mL in saline solution), 500 mL Ringer's acetate, 500 mL glucose (50 mg/mL), 500 mL mannitol (150 mg/mL), and 200 mL sodium hydrogen carbonate (500 mmol/L). Anesthesia was maintained with thiopental sodium, diazepam, fentanyl, pancuronium, and nitrous oxide in a standard combination. Heparin was administered intravenously at a dose of 4 mg/kg body weight before onset of CPB. If necessary, additional heparin was administered to maintain an activated clotting time longer than 480 seconds. No steroids were administered. Cold potassium cardioplegia was used to arrest the heart, and all operations were performed with local cooling and moderate general hypothermia (30° to 32°C). Duration of operation, CPB, and aortic occlusion was recorded. Ethylenediaminetetraacetic acid–anticoagulated blood samples were obtained at induction of anesthesia (ie, baseline), at the start of

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Table 1. Patient Characteristics and Variables Pertaining to Operation[a]

Variable	Cobe	Polystan	SciMed
Age (y)	52 (47–68)	53 (44–66)	60 (45–65)
Preoperative LV ejection fraction	0.51 (0.39–0.70)	0.66 (0.44–0.85)	0.64 (0.43–0.76)
No. of grafts	3 (1–4)	3 (1–4)	2 (2–3)
Operation time (min)	213 (173–310)	194 (145–245)	185 (159–278)
CPB time (min)	98 (66–130)	84 (54–117)	80 (68–152)
Aortic occlusion (min)	48 (24–69)	41 (16–79)	40 (26–92)

[a] Values are medians and 95% nonparametric confidence intervals. The differences between the groups were not statistically significant for any variable.

CPB = cardiopulmonary bypass; LV = left ventricular.

operation, immediately before and after 30 and 60 minutes of CPB, during closure of the sternum, every 4 hours postoperatively for 24 hours, and every 6 hours for the next 24 hours. All samples were kept on ice for a short time until analysis or centrifugation. Plasma was stored at −70°C.

The three groups were comparable with respect to patient characteristics and variables pertaining to the operation (Table 1). Three patients were excluded from postoperative follow-up because of reoperation or need for intraaortic balloon counterpulsation. The study was approved by the regional ethical committee on September 16, 1987.

Analysis of Samples

C3 activation was measured in a double-antibody enzyme immunoassay [7] specific for a C3 neoepitope (ie, antigenic determinant present in activation products, but not in the native component) expressed on C3b, iC3b, and C3c. The terminal complement complex (TCC) was quantified in a similar enzyme immunoassay [8] specific for a neoepitope expressed only in activated C9. In both assays, zymosan-activated serum was used as a standard, defined as containing 1,000 arbitrary units (AU) per milliliter.

The number of white blood cells and the hemoglobin (Hb) concentrations in the samples were determined in an electronic counter (Coulter Electronics, Harkenden, England). The percentage of neutrophil granulocytes was calculated from May-Grünwald/Giemsa–stained blood smears.

The results were corrected for hemodilution during CPB by multiplication with the factor: initial Hb/sample Hb. The Friedman test [9] was used for statistical analyses of time-dependent variable changes within each group. The Kruskal-Wallis test [9] was applied for intergroup comparisons. Results are presented as median based on Walsh numbers, with 95% nonparametric confidence intervals in parentheses.

Results

In all oxygenator groups, C3 activation products increased almost linearly after onset of CPB (Fig 1). Maximal concentrations, approximately ten to 16 times baseline, were found at closure of the sternum. Baseline levels were reestablished within 12 to 16 hours postoperatively. The maximal increase in C3 activation products was 213.3 (161.2 to 287.2) AU/mL in the SciMed group, which was significantly higher than in the Cobe group (117.5 [92.5 to 145.2] AU/mL) and the Polystan group (120.5 [95.1 to 151.8] AU/mL) ($p < 0.01$).

The concentration of the TCC also increased almost linearly from onset of CPB (Fig 2). Peak levels at closure of the sternum were approximately six to nine times baseline. Preoperative concentrations were reestablished 12 to 16 hours postoperatively. A second, moderate increase in TCC formation began approximately 36 hours postoperatively. Maximal TCC increase was 5.4 (3.7 to 7.2) AU/mL in the Cobe group, 6.6 (5.1 to 8.3) AU/mL in the Polystan group, and 7.7 (5.2 to 11.1) AU/mL in the Sci-Med group. The differences were not significant ($p = 0.26$).

There were no significant differences in neutrophil counts among the three groups. After a slight increase from baseline during the first part of the operation, the counts decreased significantly after onset of CPB ($p < 0.05$) (Table 2). Thereafter, the neutrophil counts increased throughout the operation and remained elevated during the first 48 postoperative hours ($p < 0.0001$).

Comment

In the present study, the membrane oxygenator (SciMed) was a significantly more potent C3 activator than two bubble oxygenators (Cobe and Polystan). There were no differences in TCC formation or neutrophil counts. Different polymer materials used in extracorporeal devices have a varying potential to activate complement [10]. Our findings are not explained by differences in blood contact materials [4].

Previous in vivo comparisons of bubble and membrane oxygenators have led to conflicting conclusions with respect to complement activation. Cavarocchi and colleagues [11] reported higher concentrations of C3a with a bubble oxygenator than with a membrane oxygenator. This is in agreement with the results of Tamiya and co-workers [5], which showed higher C4a, C3a, and C5a generation with a bubble than with a membrane oxygenator if bypass time exceeded 90 minutes. In several other studies, however, no differences were reported [12, 13]. One investigation provided indirect evidence of greater C5 activation with a membrane oxygenator [14]. Unequal

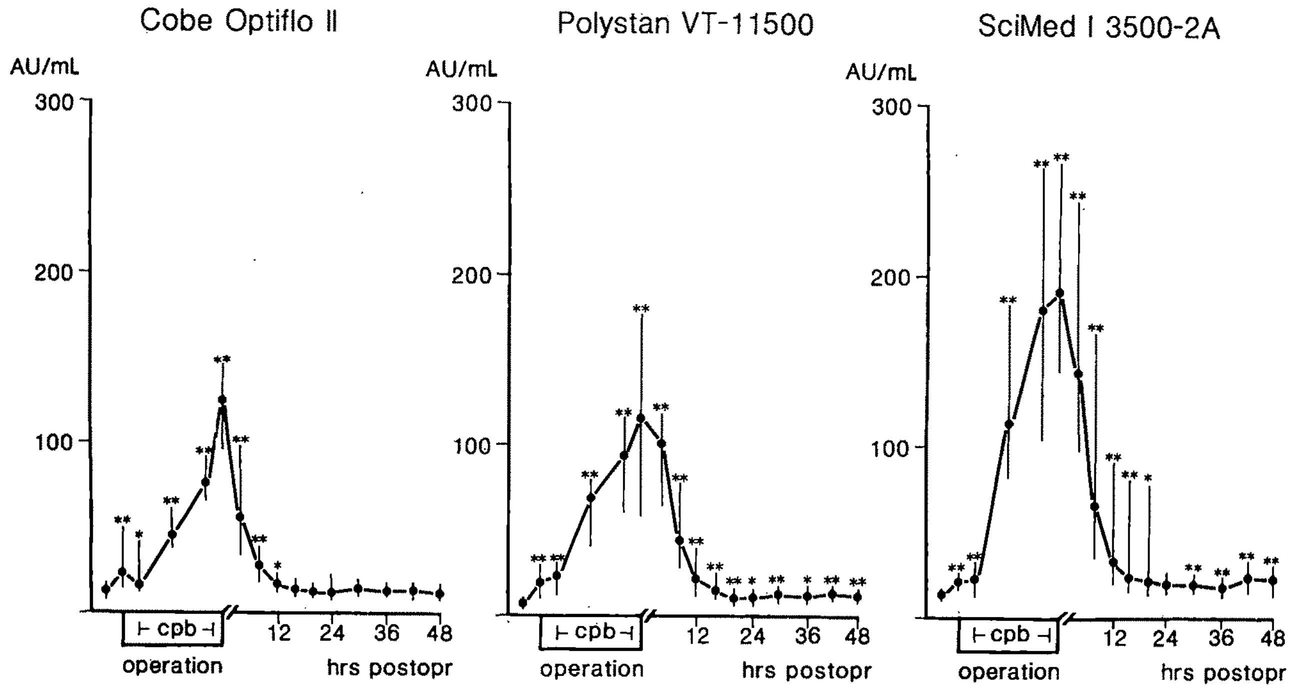

Fig 1. Concentration of C3 activation products (AU/mL) during coronary bypass operations with three different oxygenators and during the first 48 postoperative hours (median and 95% confidence interval). Note change in scale on x-axis. Significant increase from baseline sample at induction of anesthesia: *$p < 0.05$, ***$p < 0.001$. (cpb = *time on cardiopulmonary bypass.)*

trial sizes; use of varying makes of oxygenators; differences in degree of hypothermia and hemodilution [2], heparin dosage [2], and constitution of priming solutions [5, 6]; and varying sensitivity of methods used for estimation of complement activation may explain the conflicting conclusions in part. Direct comparison should therefore

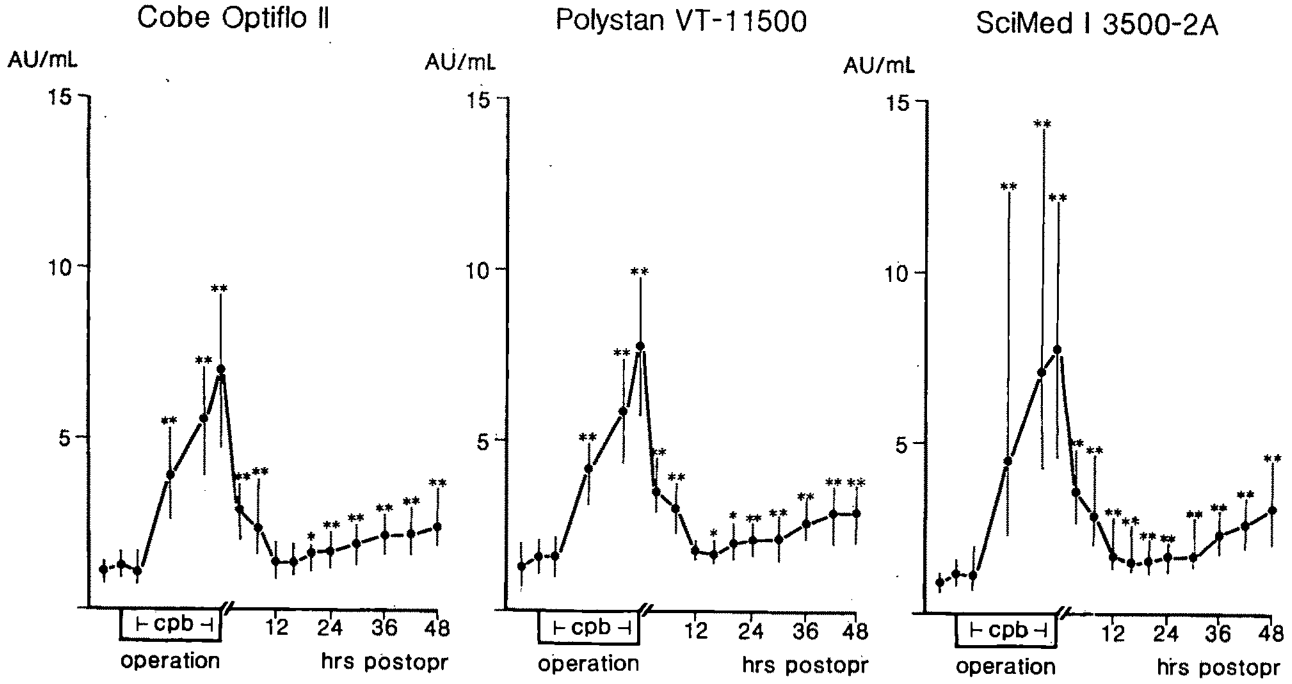

Fig 2. Concentration of terminal complement complex (AU/mL) during coronary bypass operations with three different oxygenators and during the first 48 postoperative hours (median and 95% confidence interval). Note change in scale on x-axis. Significant increase from baseline sample at induction of anesthesia: *$p < 0.05$, ***$p < 0.001$. (cpb = *time on cardiopulmonary bypass.)*

Table 2. Neutrophil Counts During and After Aortocoronary Bypass Operation[a]

Time	Cobe	Polystan	SciMed
A: Baseline	4.0 (3.2–5.6)	3.8 (2.9–4.9)	3.4 (2.7–4.4)
B: Immediately before CPB	5.2 (3.5–7.7)	4.9 (3.9–5.7)	4.3 (3.4–5.2)
C: 30-min CPB	2.9 (1.8–4.2)	2.7 (1.8–4.0)	2.8 (1.9–3.7)
D: Closure of sternum	11.0 (7.0–14.6)	9.2 (6.5–12.0)	11.2 (9.5–14.9)
E: 24 h after operation	11.0 (7.2–15.3)	10.7 (9.4–11.9)	10.5 (8.9–14.4)
F: 48 h after operation	10.5 (8.1–12.3)	11.9 (8.0–14.4)	11.7 (10.0–14.7)

[a] Values are medians and 95% nonparametric confidence intervals. Statistical comparison within each group (Friedman test): A versus B, not significant; A versus D, E, F, $p < 0.0001$; B versus C, $p < 0.05$.

CPB = cardiopulmonary bypass.

be made with caution. Considering the significant differences in C3a formation between nonporous and microporous membrane oxygenators reported by Clancy and co-workers [15], classification of oxygenators merely as bubblers or membrane oxygenators also appears to be inadequate. This view is supported by our previous in vitro findings [4].

During earlier in vitro testing, there was no C3 activation with the soft-shell bubble oxygenator (Polystan) and significant activation with the hard-shell bubble (Cobe) and the nonporous membrane (SciMed) oxygenators [4]. The relationship of maximal increase of C3 activation products between the Polystan, Cobe, and SciMed groups was 1:7.8:11 in vitro and 1:1:1.8 in vivo, which requires explanation.

Vigorous bubbling of pure oxygen through heparinized blood leads to a time-dependent generation of C3a, C4a, and C5a [5], which is probably caused by aggregated denatured immunoglobulins [5, 12]. The in vitro study was performed without oxygenation of the blood or administration of protamine. Even in this setting, a small degree of protein denaturation may occur at the blood–polymer interface [16] or in areas with blood–air contact [17]. In areas of sudden velocity changes causing disturbed flow, the formed elements of blood collide with one another, which leads to injury of erythrocytes, leukocytes, and platelets [18]. Lipid cellular debris [19] and homogenized tissue [20] are both potent complement activators. Another possible source of complement activation may therefore be substances released from damaged blood cells.

The Polystan oxygenator is virtually a large collapsible reservoir. In the noncollapsible Cobe oxygenator, blood flows by gravity from the top to the outlet near the bottom. These differences in construction, creating varying degrees of blood–air interface and velocity changes, may contribute to the unequal C3 activation in vitro. During in vivo use, however, C3 activation caused by oxygen bubbling and heparin–protamine interaction appears to become relatively much more important, resulting in equivalent formation of C3 activation products with the two bubble oxygenators. In the SciMed oxygenator, on the other hand, blood velocity at the inlet and outlet changes markedly. The membrane surface area is large, possibly permitting more extensive protein denaturation. In addition, activation of the alternative pathway caused by foreign surfaces is a function of area per milliliter of plasma [10]. Together these factors may explain the substantial activation with the SciMed oxygenator both in vitro and in vivo.

Complement activation resulting from a common stimulus varies greatly in the same amount of plasma from different donors [10]. The relative contribution from the oxygenator, heparin–protamine complexes, patient-related factors, and other sources to the total complement activation cannot be evaluated in the present study. Use of the tested membrane oxygenator led to a 1.8 times higher maximum concentration of C3 activation products than did use of the two bubblers, however, indicating that the specific oxygenator may indeed play an important role.

We conclude that evaluation of complement activation induced by CPB oxygenators cannot be generalized to a question of bubble versus membrane oxygenation but instead necessitates testing of the individual oxygenator make under standardized conditions with sensitive complement activation product assays.

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Results of Aortic Anastomoses Made Under Tension Using Polydioxanone Suture

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After early repair of congenital cardiovascular defects, such as coarctation of the aorta, late stenosis may become a problem. Use of absorbable sutures has been shown to be superior to use of nonabsorbable sutures in allowing growth of an anastomotic site along with the individual. Some concern has been raised, however, about the potential for aneurysm formation at the site of anastomosis when absorbable sutures are used. This study was undertaken to observe the effects of longitudinal tension on anastomoses made with absorbable polydioxanone suture in growing animals. Six piglets (aged 3 to 4 weeks) underwent a 1-cm resection of the infrarenal aorta and reanastomosis with polydioxanone suture. One animal died prematurely of respiratory illness. The 5 remaining animals were killed after 6 months. The excised aortas demonstrated no stenosis, no dilatation, and no burst-test failure to 250 mm Hg. Histological examination showed disrupted elastic laminae without thinning of aortic wall in all samples of aorta. We conclude that polydioxanone suture is a suitable suture material for vascular anastomoses made under tension where growth of the anastomotic site is expected.

(Ann Thorac Surg 1990;50:392–5)

Many infants with congenital cardiac defects require surgical intervention. The excellent immediate results observed in these operations have followed improvements in cardiopulmonary bypass, surgical techniques, and postoperative management. Stenosis of the anastomotic site, however, may be a problem if it fails to grow in proportion to the patient. Use of absorbable sutures has been shown to be superior to use of nonabsorbable polypropylene in allowing growth of aortic anastomoses [1–5]. Some investigators have shown that use of absorbable sutures for aortic anastomoses in growing animals over a 6-month period is associated with dilatation of the anastomotic site [1, 2].

This study was undertaken to observe the effects of tension on the growth of an aortic anastomosis made with absorbable polydioxanone suture (PDS). The shortened abdominal aorta in piglets was used as the experimental model to create longitudinal tension on a growing anastomotic site. Studies using PDS in anastomosis of the nonshortened aorta, performed in our laboratory several years ago, will be used for control comparison.

Material and Methods

Six weanling piglets, aged 3 to 4 weeks, were used for the protocol. All piglets received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 80-23, revised 1978). The young piglets, with a mean body weight of 9.2 ± 0.58 kg (mean ± standard error of the mean), were anesthetized with halothane. After endotracheal intubation, the left flank was prepared in sterile fashion and the abdominal aorta was exposed retroperitoneally. The aorta was dissected from surrounding tissues from the level of the renal arteries to the aortic bifurcation. After anticoagulation with heparin (100 U/kg), a 1-cm section of aorta was removed approximately 1.5 cm below the origin of the renal arteries. Continuity of the aorta was restored with an end-to-end anastomosis using 6-0 PDS (Ethicon, Somerville, NJ) in a continuous running technique. After closure of the incision, the animals were observed for 48 hours and then put out to pasture for 6 months.

At the end of the study, the animals were weighed and killed with an intravenous solution (Sleep-Away, Fort Dodge Laboratories, Inc, Fort Dodge, IA). The abdominal aorta was carefully removed from each animal, and all branches were ligated. Each aorta was inflated with roentgenographic contrast solution to an intraluminal pressure of 100 mm Hg. The inflated aorta was studied radiographically in simulated anteroposterior and lateral views. Measurements of the diameter of the aortic lumen were taken from the radiographs at the anastomotic site as well as at 1 cm proximal and 1 cm distal to it.

Burst-testing of each aorta was performed at an intraluminal pressure of 250 mm Hg. The aortas were opened longitudinally, and photographs were taken of the luminal surfaces.

Each aorta was fixed in 10% buffered formalin, and

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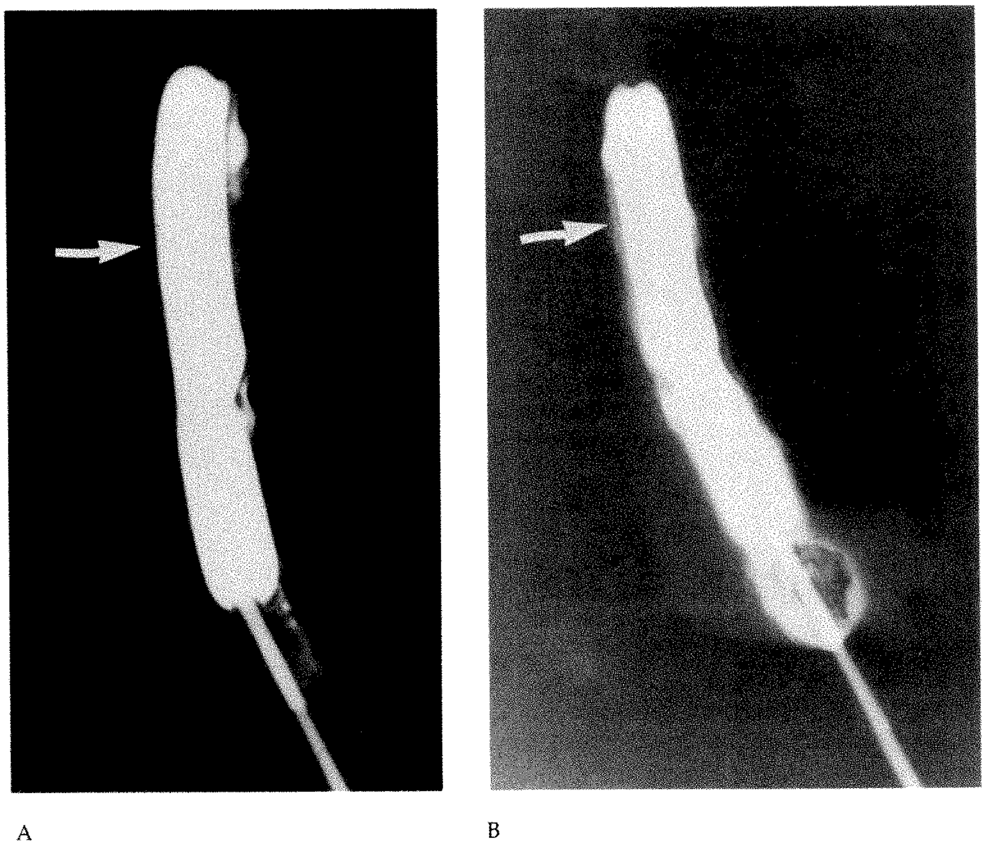

Fig 1. Representative photographs of simulated anteroposterior (A) and lateral (B) view roentgenograms of explanted, contrast-inflated aorta. The arrows *indicate the site of reanastomosis.*

representative sections were taken from the anastomotic site. The sections were examined by routine light microscopy with hematoxylin and eosin and elastic van Gieson stains. All data were recorded as the mean ± the standard error of the mean.

Results

At 6 months after operation, the body weight of the animals had increased to 88.1 ± 1.72 kg. This was an 857.6% increase from the mean weight at the time of operation. One animal died of pneumonia 25 days after operation and was excluded from the study.

All anastomoses were patent, and no animal had radiographic evidence of stenosis or aneurysmal dilatation (Fig 1). The degree of stenosis or dilatation was calculated from measurements of the roentgenograms of the inflated aortas (Table 1). The mean proximal diameter was 11.7 ± 0.39 mm, the mean distal diameter was 11.9 ± 0.38 mm, and the mean anastomotic site diameter was 11.9 ± 0.36 mm. The percentage of difference in luminal diameter at the anastomotic site versus the average of the proximal

Table 1. Calculation of Anastomotic Stenosis or Dilatation at Time of Death in Piglets[a]

Pig	Diameter (mm)			Diameter Difference (%)	Area Difference (%)
	Proximal	Distal	Anastomotic		
17	10.4	10.6	10.5	+0.00	−0.01
18	11.3	11.9	12.0	+3.45	+6.94
22	12.5	11.9	12.2	+0.00	−0.06
23	12.4	12.9	12.6	−0.40	−0.83
24	11.9	12.3	12.1	+0.00	−0.03
Mean				+0.60	+1.20

[a] Measurements taken from roentgenograms inflated with contrast solution at 100 mm Hg. A plus sign indicates a relative increase; a minus sign indicates a relative decrease in aortic diameter.

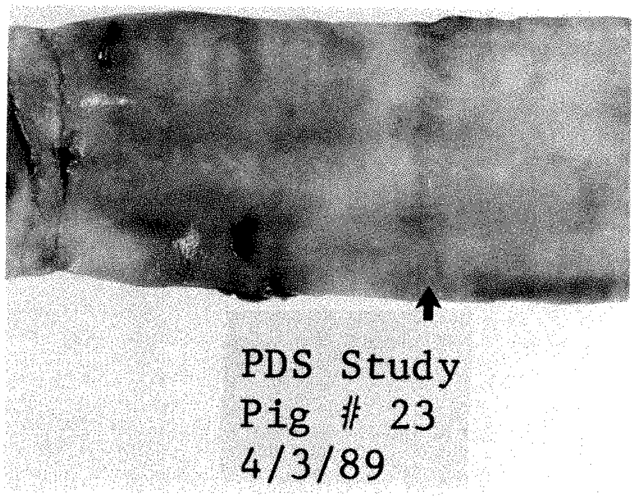

Fig 2. Luminal surface of a representative aorta. The arrow *indicates the site of reanastomosis.*

and distal diameters was calculated. The mean anastomotic diameter was 0.6% larger than the average diameter. The cross-sectional area at the anastomotic site was calculated to be 1.2% larger than the average of 1 cm proximal and 1 cm distal cross-sectional areas.

None of the aortas failed burst-testing to 250 mm Hg. After incision, the intima appeared smooth and no suture material or thrombus was visible (Fig 2). The anastomotic site was indistinguishable on the serosal surface as well as on the luminal surface in all animals.

Histological examination showed intimal thickening and fibrosis at the anastomoses (Fig 3). The thickness of the aortic wall at the point of anastomosis was estimated to be 80% to 90% of that of adjacent aorta. This reduction was no greater than 1 mm along the length of the aorta in any of the samples and involved only the immediate anastomotic region and not the adjacent aortic wall. Suture remnants were discovered in three of the samples with accompanying granulomatous foreign body reactions. With van Gieson stain for elastic fibers, all samples showed disrupted elastic laminae.

Comment

The results obtained in this study were similar to those of work previously done in our laboratory with PDS anastomoses in the abdominal aorta at 6 months [3, 5]. In the previous study, no stenosis or dilatation was noted. There were no burst-test failures, and gross and histological examinations demonstrated similar changes at 6 months.

Use of nonabsorbable sutures in pediatric cardiovascular operations, especially in children aged less than 1 year, may be a major factor in the development of anastomotic stenosis. Use of absorbable sutures for vascular operations began with catgut and provided good results both experimentally [6] and clinically [7]. This was followed by good experimental results with multifilament synthetic absorbable sutures, such as polyglycolic acid (Dexon) [4] and polygalactin (Vicryl) [5]. These sutures tended to drag when passed through the vessel wall. Furthermore, concern about the introduction of bacteria within the braids of these sutures and premature loss of strength at a suture site precluded clinical use of these materials in cardiovascular procedures.

Two newer monofilament absorbable sutures, polyglyconate (Maxon) and PDS, are free of interstices and demonstrate superior strength characteristics over time [8]. In addition, the monofilament varieties have good handling characteristics and less tissue drag than braided sutures.

A comparison between polyglycolic acid suture and nonabsorbable polypropylene suture showed that the integrity of an anastomosis is dependent on healing rather than on the permanent strength of suture material [9]. Polydioxanone has been shown to maintain the integrity of a vascular anastomosis until sufficient healing has occurred.

In growing pig models, PDS has been used in end-to-

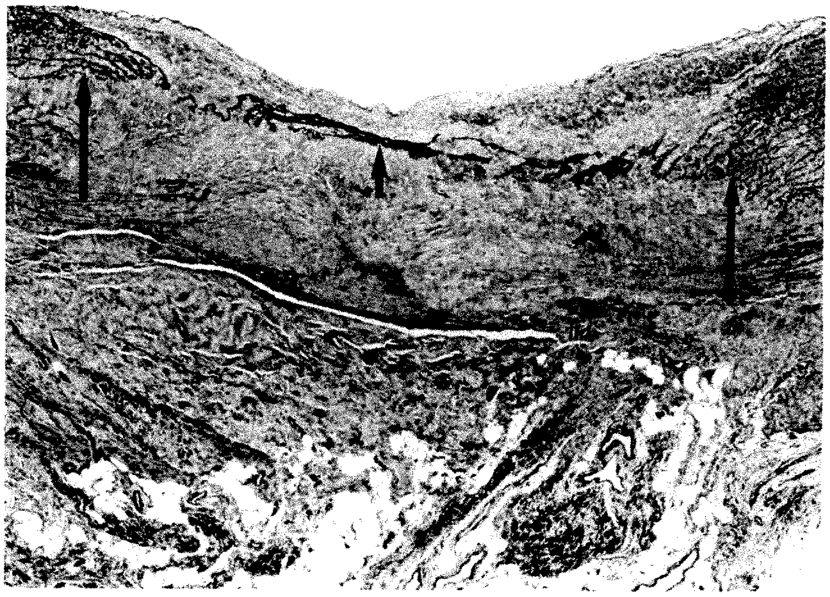

Fig 3. Site of aortic anastomosis shows extensive destruction of elastic fibers and replacement of the media by dense collagenous tissue. Intact elastic membranes are visible at each edge of the anastomotic site (long arrows) *and fragments of residual coarse black-staining fibers* (short arrows) *are visible in the center (elastic van Gieson, ×50 before 39% reduction).*

end anastomoses of the abdominal aorta with no evidence of stenosis after 6 months [1, 3, 5, 10]. Two studies using PDS and Maxon have shown a 93% [1] and 80% [2] incidence, respectively, of dilatation at the anastomotic site after 6 months. In the study using PDS, a 2-mm ring was excised from the aortas of 10 pigs, in contrast to the 10-mm ring excised in our study. Thus, these aortas had substantially less tension on the suture line than in our animals. Both experiments showed thinning of the aortic wall in the area of the anastomosis; our study did not. The difference between the results in these two studies and ours can be explained only on the basis of technique. Perhaps the suture bites were too small.

Although our experiment showed a 0.6% increase in the anastomotic diameter versus the average of the proximal and distal diameters, the gross and histological findings did not show any thinning of the aortic wall at the anastomosis. Previous anastomoses, performed in our laboratory without aortic resection, failed to demonstrate any dilatation at the anastomosis.

Certain vascular procedures, eg, end-to-end anastomosis for repair of coarctation of the aorta and arterial switch operation for transposition of the great arteries, require that an anastomosis be performed, often under some tension.

Piglets were chosen as the experimental animal for this study because they have been shown to double and triple their aortic diameter between the ages of 6 weeks and 6 months, which is similar to the increase in aortic diameter of humans from birth to maturity. In addition, the histological characteristics of pig aorta are similar to those of human aorta [11, 12]. In our study, the anastomoses were subject to the demands of this rapid growth rate as well as to the forces generated by shortening the aorta. We found no evidence that PDS had failed to meet these demands. We conclude that PDS is a suitable suture material for vascular repairs under tension. In addition, PDS demonstrated excellent characteristics in maintaining these repairs while allowing growth of the vascular anastomosis.

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Long-Term Prosthesis-Related and Sudden Cardiac-Related Complications After Valve Replacement for Aortic Stenosis

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Predictability of prosthesis-related and sudden cardiac-related complications was examined in 630 patients who were alive 30 days after valve replacement (1965 to 1986) for aortic stenosis. Follow-up totaled 4,072 patient-years. A variety of prosthetic valves, mainly mechanical, were used. The Cox regression model was used to identify independent risk factors and to estimate predicted event-freedoms relative to combinations of these risk factors. There were no risk factors for endocarditis (0.5 ± 0.1 [number of events per 100 patient-years ± the standard error]). Except for "other" prosthesis-related complications (0.4 ± 0.1), adversely influenced by porcine bioprostheses (n = 15) and by the Lillehei-Kaster prosthesis (n = 25), only factors underlying diseased preoperative patient/cardiac status had predictive influence. Predicted 10-year event-freedoms for low-risk versus high-risk estimate were 86% versus 73% for thromboembolism (1.7 ± 0.2), 95% versus 32% for anticoagulant-related hemorrhage (2.4 ± 0.2), 69% versus 36% for all prosthesis-related complications (5.0 ± 0.4), 93% versus 0% for sudden cardiac-related events (myocardial infarction and arrhythmia) (1.8 ± 0.2), and 66% versus 0.5% for combined prosthesis-related and sudden cardiac-related morbidity and mortality (6.8 ± 0.4). In 193 patients with coronary arteriography, coronary artery disease was a significant risk factor for each of the complication modalities examined except other prosthesis-related complications, prosthesis replacement, and endocarditis. Deciding to operate early in the course of aortic stenosis might "actively" reduce the rate of these complications.

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Late prosthesis-related complications are accepted as the ultimate measures of performance of aortic valve prostheses. Traditionally, emphasis has been put on the prosthetic valve as the primary determinant for thromboembolic and other complications. More recently, however, it has been increasingly recognized that patient-related or cardiac-related variables can exercise a significant modifying influence [1–6]. In this connection, sudden unexpected late deaths, constituting a relatively large fraction of the deaths in some studies [3, 7], represent a problem. In the absence of a postmortem examination, the true cause of death can be impossible to determine.

Using the proportional hazard regression model introduced by Cox [8], Lund [9] has recently been able to show that long-term survival after valve replacement for aortic stenosis (AS) during a 22-year period was unrelated to the prosthetic device. A prognostic index based on the preoperative clinical and hemodynamic profile stratified the patients into risk groups with observed/predicted 15-year survivals ranging from 90%/86% to 4%/1%. The low-risk and high-risk index also significantly separated the patients in regard to the rate of nonfatal sudden and unexpected morbidity [9]. Early operative intervention resulted in a normal age-specific, sex-specific, and operative-year–specific life expectancy [9].

The aim of the present study was to identify independent determinants of long-term prosthesis-related and sudden cardiac-related morbidity and mortality in the patients with AS already mentioned who had valve replacement in a 22-year period. For each of the specific events, we wanted to estimate both the observed cumulative event-freedoms of the patients stratified according to the identified risk models and the predicted event-freedoms that can be estimated from the Cox model relative to the same risk strata [9].

All patients were included in the present study, including those who received prosthetic valves that today are obsolete or bioprostheses that were used only sporadically. The rationale for this is related to our wish to emphasize the patient and to include as long a follow-up as possible.

Material and Methods

A total of 690 patients had valve replacement for AS performed at our institution during the 22-year period January 1965 through December 1986. The 30-day mortality was 20% (n = 20) for the first 100 consecutive patients, 7.8% (n = 38) for the ensuing 490, and 2% (n = 2) for the

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last 100 patients. This report deals with the 630 patients who were alive 30 days after operation.

Preoperative heart catheterization was performed in 605 patients, and 25 were evaluated (1985 and 1986) by Doppler echocardiography only. Peak-to-peak systolic aortic valve gradient or peak systolic Doppler gradient (used as an estimate of peak-to-peak gradient) exceeded 50 mm Hg in 590 patients. Twenty-six patients with gradients of 35 to 49 mm Hg and 14 (without Doppler echocardiography) in whom catheter access to the left ventricle was not obtained had narrow calcific stenosis at operation and symptoms placing them in New York Heart Association functional class III or IV. For the purpose of the present risk analyses, the latter 14 patients had a gradient value of 95 mm Hg (mean value of the rest of the patients) arbitrarily assigned.

Trivial aortic regurgitation (grade 1+ or 2+) at aortic root angiography [10] or at Doppler examination was observed in 80 patients. From 1975 onward, coronary angiography was performed in 193 patients (coronary angiography group) who had angina pectoris as a limiting symptom. Coronary artery disease (CAD), defined as a fixed luminal diameter reduction of 50% or more of a major coronary vessel or a first branch of a major vessel, was present in 76 patients (single- or double-vessel disease in 50 and triple-vessel or left main disease in 26).

Preoperative Variables

The variables examined are listed in Appendix 1. Left ventricular failure was defined as pulmonary edema, pulmonary vascular stasis confirmed by auscultation and roentgenography within 1 year before operation, or both conditions. Right ventricular failure was defined as crural edema, a palpable liver, ascites, or a combination of these also within 1 year preoperatively. Antianginal or antiarrhythmic drug treatment included nitrates, calcium-channel blockers, β-blockers, quinidine, and disopyramide phosphate. Systemic hypertension was recorded if it had been medically treated, and previous myocardial infarction was noted when there was electrocardiographic (ECG) and serum enzyme (creatine kinase or lactate dehydrogenase) verification. Arrhythmia was recorded if the preoperative standard resting electrocardiogram did not show sinus rhythm, and ventricular ectopic beats were noted if they constituted at least 10% of the beats in the electrocardiogram. The ECG hypertrophy score was calculated according to Romhilt and Estes [11]. Kidney failure was defined as serum creatinine level exceeding 110 μmol/L (1.24 mg/dL) in at least two successive blood samples.

Operation

Our standardized operative technique included total cardiopulmonary bypass with a bubble oxygenator, topical cooling, and (from 1977) topical and general hypothermia. Crystalloid cardioplegia with Bretschneider procaine hydrochloride–containing solution No. II or III [12] or histidine-tryptophane (HTP)–buffered solution [13] was used in all patients. Preinfusion (before infusion of the crystalloid cardioplegic solution) of cold blood (1,000 mL at 4°C; 50% full blood and 50% Ringer's chloride) was used until 1983. Details of cardiopulmonary bypass, cardioplegia, and prosthesis implantation technique have been described elsewhere [3, 9, 14]. The surgical team and technique remained largely unchanged throughout the period. The majority of the operations were performed by one of us (O.K.A.).

Operation-related variables and the prosthetic valves used are listed in Appendix 1. Carpentier-Edwards (n = 10) and Hancock (n = 5) valves constituted the porcine bioprostheses. Concomitant coronary artery bypass grafting using the saphenous vein was performed in 53 patients, and an ascending aortic prosthesis was implanted in 2 patients. No other associated surgical procedures were undertaken.

Eight of the 15 patients who received a bioprosthesis were put on a lifelong regimen of low-dose acetylsalicylic acid. All other patients were prescribed lifelong Coumadin (crystalline warfarin sodium) treatment with the goal of maintaining Owren's prothrombin-proconvertin index within the 10% to 20% range. Treatment was centralized at one hospital in each of the counties using our cardiac surgical service. The short geographical distances in Denmark and the fact that the treatment was without financial cost to the patients permitted frequent control visits [4].

Follow-up

All patients were seen annually at the cardiology outpatient clinic. A computerized register covering all hospital contacts in our catchment area as well as the national personal register (both including updated accounts of vital status, address of patient and of primary physician, ongoing or previous hospital admission, and place of death if applicable) were checked for additional information. Records from other hospitals were procured and the primary physician was contacted when necessary. With the closing date for follow-up being December 1987, a total of 4,072 patient-years at risk (mean follow-up, 6.5 years; range, 0.1 to 21.0 years with a minimum follow-up of 11 months for patients still alive) had been accumulated. A total of 176 patients had died; death certificates were available for all and autopsy reports for 91. No patient was unaccounted for.

Prosthesis-Related and Sudden Cardiac-Related Morbidity and Mortality

Our aim was to examine sudden events that were probably directly related to the prosthetic valve or to the degree of preoperative damage to the heart and not to the operation, intraoperative myocardial anoxia, or related postoperative complications. Accordingly, we chose to include events that occurred after the first 30 postoperative days only. However, none of the patients experienced prosthesis-related events within the first 30 days.

Our definitions of the events have been described previously [3–5] and follow recent guidelines given by The Society of Thoracic Surgeons [15]. Thromboembolism encompassed all systemic vascular events including transitory cerebral ischemia unless proven to be of thrombotic (postmortem examination or carotid angiography) or hemorrhagic origin. Anticoagulant-related hemorrhage included all bleeding episodes: gastrointestinal bleeding (eg, from peptic ulcers), macroscopic hematuria, cerebral hemorrhage, and nontraumatic subcutaneous ecchymoses and epistaxis necessitating treatment. This definition is more liberal than that of The Society of Thoracic Surgeons [15], as some of the bleeding episodes did not cause death, stroke, operation, or hospitalization or necessitate transfusion.

Prosthetic valve endocarditis was considered present in the case of clinical sepsis with positive cultures or verification at prosthesis replacement or postmortem examination. Intravascular hemolysis [6] was defined as anemia unrelated to bleeding and not reversible and controllable by iron, vitamin B_{12}, or folic acid substitution. Paravalvar leak was diagnosed at aortic root angiography, Doppler echocardiography, prosthesis replacement, or postmortem examination. Death due to acute regurgitation in 2 patients whose prosthesis was detached for half the circumference of the annulus was included as paravalvar leak (microscopy and culture of material from the annulus and prosthesis did not reveal signs of endocarditis). Primary tissue failure of bioprostheses with or without calcification included structural defects, tear, perforation, and fibrosis of the valve leaflets in the absence of endocarditis. Other complications included a myocardial infarction caused by the sewing ring of a Lillehei-Kaster prosthesis compromising a coronary ostium, and hemodynamic malfunction (transprosthesis gradient of 65 mm Hg) of a 21-mm Lillehei-Kaster valve.

Sudden cardiac-related events (absence of possible prosthesis-related cause) included myocardial infarction with typical ECG changes, serum enzyme elevations (creatine kinase or lactate dehydrogenase), and typical symptomatology (at least two of these three criteria) or verified at postmortem examination, and arrhythmia (including sinoatrial and atrioventricular conduction block) causing death or necessitating pacemaker implantation. In the case of a fatal arrhythmia outside the hospital and without a postmortem examination, the distinction from stroke was based on the immediate circumstances surrounding the death and the recent patient history (contact with the physician who wrote the death certificate).

Statistical Analysis

All tests were computerized using the BMDP software package [16]. Comparisons between groups were performed using the standard χ^2 test or the nonpaired *t* test when appropriate. Linearized complication rates (number of events per 100 patient-years at risk) ± one standard error were calculated as described by Grunkemeier and colleagues [17]. The Kaplan-Meier product-limit method was used in the construction of the cumulative event-free curves, and differences between curves were tested by the log-rank test. For identification of independent risk factors for prosthesis-related and sudden cardiac-related events, the proportional hazard regression model introduced by Cox [8] was used. Descriptions of the Cox model, of our formalized test sequence, and of the method used to test the prerequisite of proportional event-rates of each of the risk factors included in the final Cox model have been given in detail previously [3, 9].

Quantitative variables (including year of operation) were categorized into "high" versus "low" values using different cutoff points; the categorized forms were then compared with the variable in its quantitative (continuous) form in a univariate Cox model, and the form giving the largest log-likelihood estimate was chosen for further analysis. This procedure was carried out for each of the complication modalities.

The Cox model specifies that the event-rate $\lambda(t)$ at time t after operation for a patient with risk factors $z_1, z_2, \ldots, z_p$ is given as $\lambda(t) = \lambda_o(t) \times \exp(b_1z_1 + b_2z_2 + \ldots + b_pz_p)$, where $\lambda_o(t)$ is the common underlying event-rate and $b_1, b_2, \ldots, b_p$ are the regression coefficients. It turned out that the final Cox models of the present study included only categorical variables (risk factor in question present versus absent, assigned the values 1 and 0, respectively).

Furthermore, as the regression coefficients in the models were positive, it follows that combinations of none of the independent risk variables, any one of these variables, any two, any three, and so on to all of the independent risk factors identify patient groups with increasing risk, which was checked by constructing the observed event-free curves for each of these groups. The estimated (predicted) event-freedom was calculated for each group as $S(t,\overline{RI}) = S_o(t)^{\exp(\overline{RI})}$, where $S_o(t)$ is the common underlying event-freedom and $\overline{RI}$ the mean risk index for the group; the risk index for each patient equals $z_1b_1 + z_2b_2 + \ldots + z_pb_p$. This method reuses information from all 630 patients in the calculation of the estimated event-freedom for each risk group, thus also allowing calculation of the estimated freedom for combinations of risk factors that included only a few patients or no patients.

The prognostic influence of the variables listed in Appendix 1 was examined, and the tests were performed on two populations: the total patient population and the 193 patients in the coronary angiography group in whom the possible influence of CAD and of bypass grafting could be analyzed. Cumulative event-freedoms are given with ± one standard error. The level of significance chosen was 0.05.

Results

Cumulative survival at 5, 10, and 15 years was 80% ± 3%, 62% ± 3%, and 41% ± 4%, respectively, for the 226 patients operated on during 1965 through 1976 compared with 88% ± 2% at 5 years and 79% ± 3% at 10 years for the 404 patients having operation during 1977 through 1986 ($p < 0.01$). The 176 late deaths were caused by prosthesis-related complications in 18.2%, by sudden cardiac-related events in 23.9%, by congestive heart failure in 30.1% (n = 53), and by other causes in 27.8% (cancer in 18 patients, pulmonary insufficiency or bronchopneumonia in 10, hepatic cirrhosis in 3, primary kidney failure in 4, acute pancreatitis in 2, autopsy-verified cerebral thrombosis in 4, pulmonary embolism in 1, sternal ostitis in 1, trauma in 4, and suicide in 2). Prosthesis-related and sudden cardiac-related morbidity and mortality are summarized in

Table 1. Prothesis-Related and Sudden Cardiac-Related Morbidity and Mortality

Event[a]	No. of Events[b]	Event Rate[c]	No. of Deaths[d]	Percentage of Deaths[e]
Thromboembolism	69 (55)	1.7 ± 0.2	11 (6)	6.3
Cerebral	49		8 (4)	
Extremities	11		1[f] (0)	
Central retinal artery	7		0	
Coronary	1		1 (1)	
Mesentery	1		1 (1)	
Anticoagulant-related hemorrhage	96 (66)	2.4 ± 0.2	7 (5)	4.0
Cerebral	16		6 (4)	
Gastrointestinal	41		1 (1)	
Urogenital	17		0	
Epistaxis, subcutaneous	21		0	
Vitreous body	1		0	
Endocarditis	22 (22)	0.5 ± 0.1	9 (6)	5.1
Other prosthesis-related complications	18 (16)	0.4 ± 0.1	5 (5)	2.8
Hemolysis	6		0	
Hemolysis and paravalvar leak	2		1[f] (1)	
Paravalvar leak[g]	4		2 (2)	
Coronary ostium compromised[h]	1		1 (1)	
Primary tissue failure	4		0	
Hemodynamic malfunction [i]	1		1[f] (1)	
All prosthesis-related complications[j]	205 (142)[k]	5.0 ± 0.4	32 (22)	18.2
Sudden cardiac-related events	72 (72)	1.8 ± 0.2	42 (18)	23.9
Arrhythmia				
Fatal	14		14 (8)	
Pacemaker implanted	12		0	
Myocardial infarction	46		28 (10)	
Prosthesis- and sudden cardiac-related morbidity and mortality[l]	277 (197)[m]	6.8 ± 0.4	74 (40)	42.0

[a] See text for definitions; see also Figure 1. [b] Numbers in parentheses are numbers of patients. [c] This is the number of events per 100 patient-years ± the standard error. [d] Numbers in parentheses are numbers of postmortem examinations. [e] This is based on all 176 late deaths. [f] Death occurred after prosthesis replacement. [g] Prosthesis was detached from half the circumference in 2 patients (both died; no signs of endocarditis at culture or microscopy). [h] Compromising factor was the sewing ring of a Lillehei-Kaster prosthesis. [i] This was a 22-mm Lillehei-Kaster prosthesis with a transprosthesis peak systolic gradient of 65 mm Hg. [j] This includes the preceding four categories. [k] Seventeen patients had complications from more than one of the prosthesis-related complications. [l] This includes the preceding two categories. [m] Seventeen patients had both prosthesis- and sudden cardiac-related events.

Table 1 together with the linearized event-rates; Figure 1 gives the observed cumulative event-freedoms. Structural defects (apart from cloth wear of Starr-Edwards cloth-covered valves), mechanical failure, or thrombotic occlusion of mechanical valves was not observed. The results of the Cox analysis of each event modality in the total patient population are shown in Table 2 together with the univariate significance of each of the independent risk factors.

Thromboembolism

The 69 events resulted in death in 11 instances (including one death after prosthesis replacement necessitated by recurrent embolism), cerebral sequelae in 17, and arterial embolectomy, partial unilateral blindness, or other permanent functional disability in seven, giving a linearized rate of serious events of 0.9 ± 0.1. Kidney failure had independent predictive influence (Fig 2), but type of prosthesis did not. The linearized rate was 1.4 ± 0.7 for the St. Jude valve (in use from 1980) and 1.7 ± 0.5 for the Starr-Edwards Silastic (Dow Corning) ball valve (in use from 1965 through 1973 and again from 1979). For the latter valve type, no thromboembolic events were noted after the sixth year (15-year freedom of 90% ± 3%).

The independent risk factors in the coronary angiography group were CAD ($b = 1.525$, $p = 0.04$) and previous myocardial infarction ($b = 1.423$, $p = 0.04$). Combinations of none ($n = 107$), any one ($n = 71$), and both ($n = 15$) of these risk factors resulted in observed 10-year freedoms of 98% ± 2%, 90% ± 4%, and 80% ± 10%, respectively ($p =$

0.002). Kidney failure was present in 15% (n = 17) of the patients without and in 30% (n = 23) of those with CAD ($p < 0.05$).

Anticoagulant-Related Hemorrhage

Of the 96 events, seven caused death, three resulted in cerebral sequelae, and the rest were not associated with any permanent disability. Bleeding causing death, stroke, operation, or hospitalization or necessitating transfusion [15] occurred 60 times, giving a linearized rate of 1.5 ± 0.2. The risk stratification resulting from combinations of the four independent risk factors shown in Table 2 resulted in highly significantly different bleeding rates (Fig 3).

Previous systemic hypertension (b = 0.988, $p = 0.04$) and CAD (b = 0.890, $p = 0.04$) were independent risk factors in the coronary angiography group. Presence of none (n = 107), any one (n = 76), and both (n = 10) of these factors gave observed 10-year freedoms of 92% ± 3%, 70% ± 14%, and 51% ± 19%, respectively ($p = 0.002$).

Prosthetic Valve Endocarditis

The 22 episodes of endocarditis resulted in death in 9 patients: in 2 after prosthesis replacement, which was performed in 9, and in 7 during antibiotic treatment, instituted in 13. No variables had predictive influence.

Other Prosthesis-Related Complications

Combinations of none (n = 483), any one (n = 135), and any two (n = 12) of the independent risk factors (see Table 2) gave 15-year freedoms of 98% ± 1%, 93% ± 3%, and 30% ± 23%, respectively ($p < 0.0001$). No patient had all three factors present (no bioprostheses with an orifice diameter of ≤ 15 mm compared with 25% of the Starr-Edwards Silastic ball valves, 7% of the cloth-covered valves, 32% of the Lillehei-Kaster valves, 4% of the St. Jude valves, and 0% of the rest of the valves; $p < 0.0001$). The high prevalence of an orifice diameter of 15 mm or less together with the age factor (28% of the patients who received a Lillehei-Kaster prosthesis and 33% of those who received a bioprosthesis were 45 years old or younger compared with 10% of the other patients; $p < 0.001$) probably precluded Lillehei-Kaster valves (10-year freedom of 87% ± 7%; $p = 0.02$ compared with all other valves) from having independent influence. Age of 45 years or less (b = 2.840, $p = 0.005$) and Lillehei-Kaster prosthesis (b = 3.062, $p = 0.01$) were independent risk factors in the group having coronary angiography.

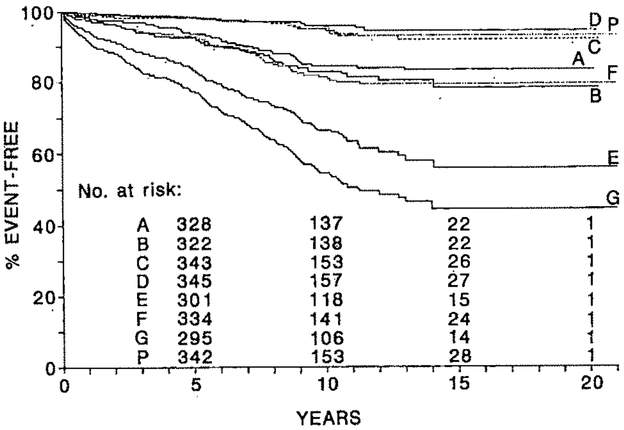


Fig 1. Cumulative observed freedom from thromboembolism (A), *anticoagulant-related hemorrhage* (B), *endocarditis* (C), *other prosthesis-related complications* (D), *all prosthesis-related complications* (E), *sudden cardiac-related events* (F), *combined prosthesis- and sudden cardiac-related events* (G), *and prosthesis replacement* (P) *(see Table 1 and text for definitions). Ten-year and 15-year event-freedoms (± the standard error) were 85% ± 2% and 82% ± 3% for A, 84% ± 2% and 78% ± 3% for B, 95% ± 1% and 92% ± 2% for C, 96% ± 1% and 94% ± 2% for D, 66% ± 3% and 56% ± 4% for E, 82% ± 2% and 79% ± 2% for F, 55% ± 3% and 45% ± 4% for G, and 95% ± 1% and 93% ± 2% for P, respectively.*

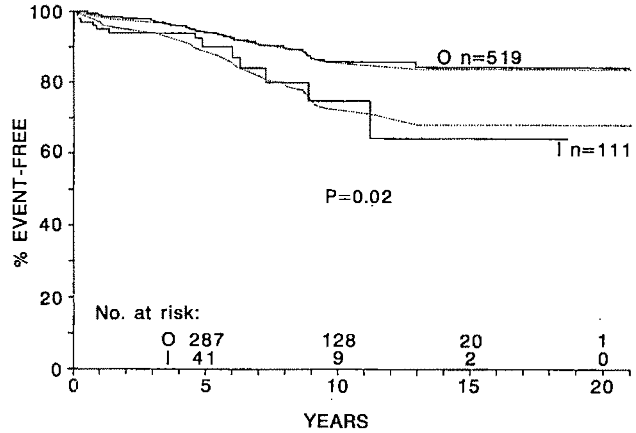


Fig 2. Cumulative observed ("step" curves) and estimated (predicted) (broken curves) freedom from thromboembolism in relation to absence (O) or presence (I) of the independent risk factor (kidney failure) identified in Table 2. Ten-year observed (± the standard error) and estimated event-freedoms were 86% ± 2% and 86% for O and 75% ± 8% and 73% for I, respectively.

Prosthesis Replacement

The underlying events leading to reoperation are included in Table 1. Reoperation was performed in 20 patients (linearized rate, 0.5 ± 0.1). It was necessary because of endocarditis in 9 (2 died), hemolysis or paravalvar leak in 5 (1 died), recurrent embolism in 2 (1 died), primary tissue failure in 3 (none died), and a hemodynamically malfunctioning Lillehei-Kaster valve in 1 (died). Patients with none (n = 524), any one (n = 99), and any two (n = 7) of the independent risk factors (see Table 2) had observed 10-year event-freedoms of 97% ± 1%, 92% ± 4%, and 43% ± 22%, respectively ($p < 0.0001$). No patient had all three factors, as none of the patients with a bioprosthesis had a preoperative gradient of less than 50 mm Hg. There were only three reoperations in the group having coronary angiography.

All Prosthesis-Related Complications

Event-freedoms relative to combinations of the two independent risk factors (see Table 2) are depicted in Figure 4. In the coronary angiography group, age of 45 years or less (b = 1.658, $p = 0.01$), CAD (b = 1.166, $p = 0.004$), and

Table 2. Independent Risk Factors for Prosthesis-Related and Sudden Cardiac-Related Morbidity and Mortality

		Significance in Cox Model			Univariate Significance		
					10-Year Cumulative Event-Freedom ± SE		
Event[a]	Risk Factor[b]	b	SE	p Value	Risk Factor Present[g]	Risk Factor Absent[g]	p Value
Thromboembolism[c]	Kidney failure	0.761	0.321	0.015	75% ± 8% (111)	86% ± 2% (519)	0.015
Anticoagulant-related hemorrhage[d]	Previous systemic hypertension	0.930	0.384	0.01	65% ± 12% (38)	85% ± 2% (592)	0.01
	Cardiothoracic index > 0.50	0.770	0.311	0.01	79% ± 3% (371)	93% ± 2% (259)	0.003
	Angina pectoris	0.684	0.297	0.02	81% ± 3% (405)	90% ± 3% (225)	0.02
	NYHA class IV	0.666	0.323	0.04	67% ± 9% (71)	86% ± 2% (559)	0.01
Endocarditis	None	...	...	...	...	...	...
Other prosthesis-related complications[e]	Porcine bioprosthesis	1.784	0.715	0.01	67% ± 21% (15)	95% ± 1% (615)	0.0003
	Prosthetic orifice diameter ≤ 15 mm	1.590	0.571	0.005	88% ± 5% (72)	98% ± 1% (558)	0.008
	Age ≤ 45 y	1.461	0.533	0.006	88% ± 5% (72)	97% ± 1% (558)	0.0001
Prosthesis replacement[f]	Porcine bioprosthesis	1.863	0.592	0.002	45% ± 21% (15)	96% ± 1% (615)	<0.0001
	Aortic valve gradient < 50 mm Hg	1.509	0.761	0.04	85% ± 11% (26)	95% ± 1% (604)	0.04
	Age ≤ 45 y	1.072	0.489	0.03	84% ± 6% (72)	97% ± 1% (558)	0.002
All prosthesis-related complications[c]	Cardiothoracic index > 0.60	0.544	0.242	0.02	48% ± 10% (62)	68% ± 3% (568)	0.02
	Prosthetic orifice diameter ≤ 15 mm	0.442	0.220	0.05	50% ± 9% (72)	68% ± 3% (558)	0.05
Sudden cardiac-related events[e]	Previous myocardial infarction	1.511	0.308	<0.0001	59% ± 10% (51)	83% ± 2% (579)	<0.0001
	Aortic valve gradient < 50 mm Hg	1.248	0.442	0.005	42% ± 17% (26)	83% ± 2% (604)	0.007
	Absence of intraoperative general hypothermia	0.692	0.285	0.02	77% ± 2% (235)	87% ± 4% (395)	0.007
	NYHA class IV	0.678	0.306	0.03	66% ± 8% (71)	84% ± 2% (559)	0.0006
	Cardiothoracic index > 0.55	0.621	0.253	0.02	71% ± 5% (167)	86% ± 2% (463)	0.0001
Prosthesis- and sudden cardiac-related morbidity and mortality[e]	Previous myocardial infarction	0.619	0.243	0.01	41% ± 10% (51)	56% ± 3% (579)	0.01
	Cause other than degenerative/unknown and rheumatic	0.612	0.164	0.0002	42% ± 6% (124)	58% ± 3% (506)	0.0005
	Cardiothoracic index > 0.60	0.576	0.213	0.007	30% ± 8% (62)	58% ± 3% (568)	0.0003
	NYHA class IV	0.429	0.215	0.04	38% ± 8% (71)	57% ± 3% (559)	0.005
	Symptom duration > 60 mo	0.306	0.153	0.04	42% ± 5% (168)	60% ± 3% (462)	0.003

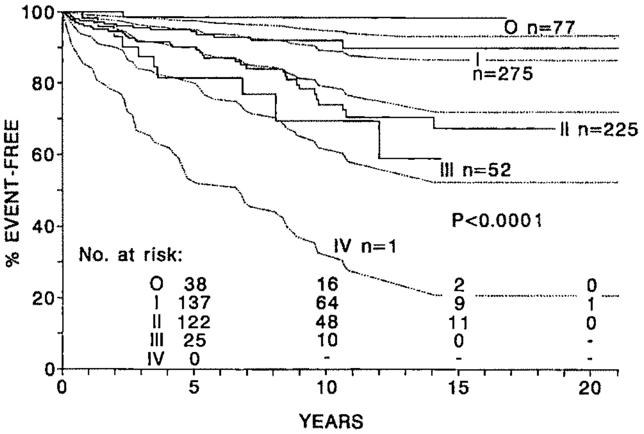
[a] See Table 1, Figures 1 through 6, and text. [b] See Appendix 1 and text. The risk factors for each event are arranged in order of decreasing predictive strength as indicated by their regression coefficient. The global χ^2 test of the final Cox models gave the following significances: [c] $p < 0.01$; [d] $p < 0.0001$; [e] $p < 0.000001$; [f] $p < 0.00001$. [g] Numbers in parentheses are numbers of patients.

b = regression coefficient; NYHA = New York Heart Association; SE = standard error.

previous systemic hypertension (b = 0.867, p = 0.05) had independent influence. Combinations of none (n = 98), any one (n = 84), and any two (n = 11) of these risk factors (no patient had all three) gave observed 10-year event-freedoms of 88% ± 4%, 53% ± 13%, and 47% ± 19%, respectively (p = 0.003).

Sudden Cardiac-Related Events

The independent risk factors (see Table 2) resulted in a highly significant risk stratification (Fig 5). Ventricular ectopic beats (b = 2.170, p = 0.04), cardiothoracic index greater than 0.55 (b = 1.487, p = 0.04), and CAD (b = 1.291, p = 0.04) were independent risk factors in the group having coronary angiography. Combinations of none (n = 101), any one (n = 83), and any two (n = 9) of these risk factors (no patient had all three) gave 10-year freedoms of 97% ± 2%, 92% ± 3%, and 40% ± 22%, respectively (p = 0.0002). Bypass grafting did not influence the sudden cardiac-related events; 53 patients with bypassed CAD (28 with single- or double-vessel disease and 25 with triple-vessel or left main disease) and 23 in whom bypass grafting was not performed (22 with single-



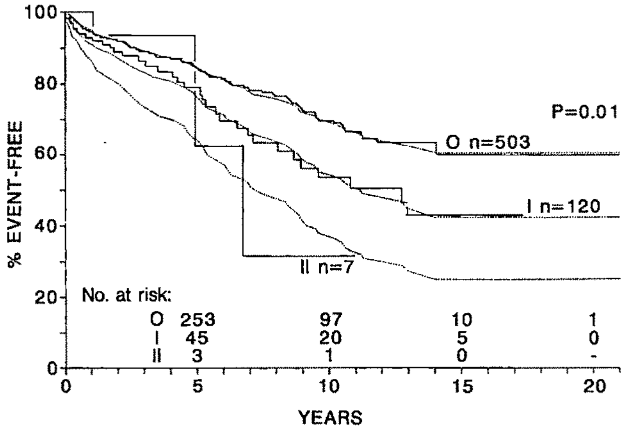
O	38	16	2	0
I	137	64	9	1
II	122	48	11	0
III	25	10	0	-
IV	0	-	-	-

Fig 3. Cumulative observed ("step" curves) and estimated (predicted) (broken curves) freedom from anticoagulant-related hemorrhage in relation to combinations of none (O), any one (I), any two (II), any three (III), and all four (IV) of the independent risk factors (previous systemic hypertension, cardiothoracic index > 0.50, angina pectoris, New York Heart Association class IV) identified in Table 2. Ten-year observed (± standard error) and estimated event-freedoms were 98% ± 2% and 95% for O, 92% ± 2% and 89% for I, 74% ± 4% and 79% for II, 70% ± 9% and 62% for III, and 1 patient with an event at 4 years and 32% for IV, respectively.

or double-vessel disease and 1 with triple-vessel disease) had comparable event-rates.

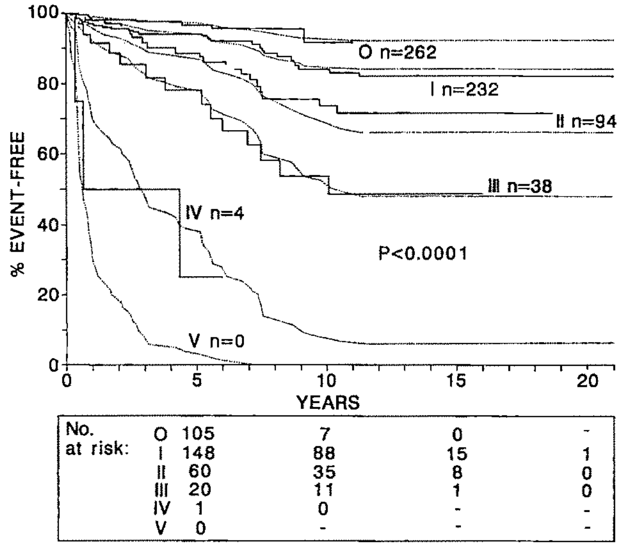
Total Prosthesis-Related and Sudden Cardiac-Related Morbidity and Mortality

The risk stratification resulting from the independent risk factors (see Table 2) is shown in Figure 6. The patients with degenerative/unknown or rheumatic cause had a mean age of 61 ± 8 years (standard deviation) compared with 50 ± 14 years for those with other causes ($p < 0.0001$).



O	253	97	10	1
I	45	20	5	0
II	3	1	0	-

Fig 4. Cumulative observed ("step" curves) and estimated (predicted) (broken curves) freedom from all prosthesis-related complications in relation to combinations of none (O), any one (I), or both (II) of the independent risk factors (cardiothoracic index > 0.60, prosthetic orifice diameter ≤ 15 mm) identified in Table 2. Ten-year observed (± standard error) and estimated event-freedoms were 70% ± 3% and 69% for O, 53% ± 7% and 54% for I, and 31% ± 12% and 36% for II, respectively.



No. at risk:				
O	105	7	0	-
I	148	88	15	1
II	60	35	8	0
III	20	11	1	0
IV	1	0	-	-
V	0	-	-	-

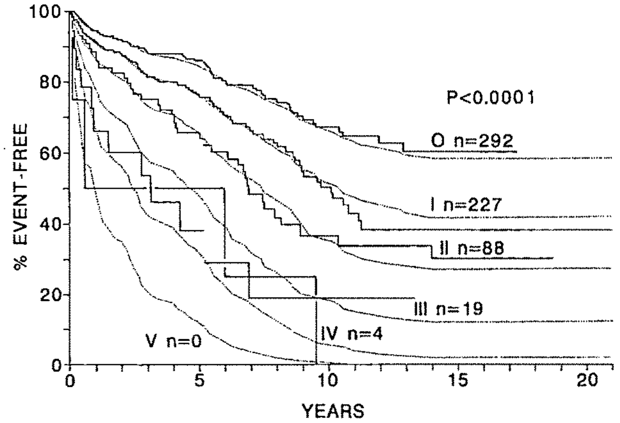
Fig. 5. Cumulative observed ("step" curves) and estimated (predicted) (broken curves) freedom from sudden cardiac-related events in relation to combinations of none (O), any one (I), any two (II), any three (III), any four (IV), and all five (V) of the independent risk factors (previous myocardial infarction, aortic valve gradient < 50 mm Hg, absence of intraoperative general hypothermia, New York Heart Association class IV, cardiothoracic index > 0.55) identified in Table 2. Ten-year observed (± standard error) and estimated event-freedoms were 91% ± 4% and 93% for O, 84% ± 3% and 85% for I, 74% ± 6% and 69% for II, 54% ± 10% and 51% for III, respectively, 8% (estimated only) for IV, and 0% (estimated only) for V.

The independent risk factors in the coronary angiography group were age less than 50 years (b = 1.737, $p = 0.001$), CAD (b = 1.288, $p = 0.003$), and digitalis or diuretic treatment (b = 1.056, $p = 0.004$). Patients with none (n = 45), any one (n = 98), and any two (n = 50) of these risk factors (no patient had all three) had 10-year event-freedoms of 90% ± 6%, 68% ± 10%, and 37% ± 11%, respectively ($p < 0.0001$).

Comment

It should be emphasized that the present material offered several advantages in addition to the long follow-up and the large number of patient-years. Not only did the surgical team and technique remain largely unchanged, but a contemporary cold crystalloid cardioplegic method [12, 13] was used consistently in all operations. By minimizing intraoperative anoxic myocardial damage [18], this served to preserve the prognostic profile of a patient to a higher degree than would have been possible if crystalloid cardioplegia, which was not introduced worldwide until late in the 1970s, had not been used. These factors probably explain to a large extent why year of operation did not independently influence any of the events of this study.

By excluding patients with substantial aortic regurgitation and associated heart diseases other than CAD, we



No. at risk:	O	152	60	7	0
	I	99	31	3	1
	II	37	13	4	0
	III	5	2	0	-
	IV	2	0	-	-
	V	0	-	-	-

Fig 6. Cumulative observed ("step" curves*) and estimated (predicted)* (broken curves) *freedom from prosthesis-related and sudden cardiac-related morbidity and mortality in relation to combinations of none (O), any one (I), any two (II), any three (III), any four (IV), and all five (V) of the independent risk factors (previous myocardial infarction, cause other than degenerative/unknown and rheumatic, cardiothoracic index > 0.60, New York Heart Association class IV, symptom duration > 60 mo) identified in Table 2. Ten-year observed (± standard error) and estimated event-freedoms were 67% ± 4% and 66% for O, 50% ± 5% and 51% for I, 37% ± 7% and 35% for II, 19% ± 11% and 18% for III, 25% ± 22% (at 9 years) and 10% for IV, respectively, and 0.5% (estimated only) for V.*

rendered the study population homogeneous in terms of interpretation of the significance of potential risk factors [3, 9, 19]. That the patients attended annual cardiology outpatient clinic control reviews, that these reviews and the centralized regulation of Coumadin treatment as well as the treatment itself were without financial cost to the patients, that the Danish health care system allows free and frequent visits to the primary physician and free hospital treatment, and that the fate of the patients in terms of hospitalization and death is registered in computerized systems greatly increase the likelihood that we have identified all events of significance for this type of study.

Given the problem associated with sudden, unexpected, and often unexplained death, we chose to include sudden cardiac-related events in our study. From the factors just mentioned we inferred that we would be able to obtain relatively reliable diagnoses, even in the absence of a postmortem examination. Death from congestive heart failure accounted for the vast majority of an accelerating late (>10 years) excess mortality in the high-risk groups of our survival analysis [9]. Furthermore, as recurrence of congestive heart failure as a morbid event after valve replacement, which we [20] have studied in some detail previously, is usually not well defined in time, we chose to exclude this event from the present study.

Comparisons between patient series of the rates of the various prosthesis-related complications are difficult, principally due to differences in patient population, length of follow-up, and quality and type of anticoagulant treatment. Macmanus and associates [21] noted a significant reduction in the linearized rate of thromboembolism for the Starr-Edwards Silastic ball valve from 5.0 per 100 patient-years for implantations during 1965 through 1972 to 3.4 for 1973 to 1979. However, the bleeding rate increased synchronously from 1.4 to 3.0. Our relatively low rates of thromboembolism and bleeding were not influenced by year of operation. Rates of 1.2 to 2.3 per 100 patient-years for thromboembolic events and of 1.3 to 7.9 for hemorrhagic events have been reported for contemporary disc valves [22–24]. As these reports in general adhered to guidelines comparable with those of The Society of Thoracic Surgeons [15] and thus did not include minor bleeding episodes, our rates of thromboembolism and hemorrhage compare favorably with those mentioned here. This should be viewed in light of the fact that 48% of the prosthesis types included in our study (the Starr-Edwards cloth-covered and track valves, the Smeloff-Cutter valve, and the Lillehei-Kaster valves) are obsolete. The combined rate of all prosthesis-related complications, 3.9 to 5.9 per 100 patient-years for the porcine bioprosthesis and 3.5 to 12.3 for the Björk-Shiley and St. Jude disc prostheses [22–24], probably gives a better estimate of overall prosthesis performance. Excluding the 36 minor bleeding events in this report, our comparable rate becomes 169 events per 4,072 patient-years or 4.2 per 100 patient-years.

The consequences of the complications examined in the present study varied considerably. Only 10% of the hemorrhagic episodes resulted in death or permanent functional disability, whereas the thromboembolic events were of transient and benign nature in only 47%. These findings are in agreement with those of others [25]. Prosthetic valve endocarditis and the other prosthesis-related complications resulted in death or reoperation in more than two thirds of the patients, and almost 60% of the sudden cardiac-related events were fatal. A reduction in these events would consequently improve both longevity and quality of life for the patients.

The main result of the present study was the identification of risk models for the various events that stratified the patients into groups with widely differing observed and predicted event-freedoms. The risk models predominantly emphasized diseased preoperative patient/cardiac status as the most decisive factor. Apart from the demonstration of the well-known drawbacks of porcine bioprostheses and small Lillehei-Kaster prostheses in regard to other prosthesis-related complications and reoperation, no prosthesis type had any independent influence. The significance of each individual risk factor should be interpreted with some caution. With more than 30 variables (see Appendix 1) used as potential predictors of eight events (see Table 2), we have a multiple testing problem; some of the risk factors with p values greater than 0.01 would probably not reappear in a second data set/patient series.

To our knowledge, only McGoon and co-workers [26] have also performed a multivariate examination of the relation between prosthesis-related complications and patient-related factors in a homogeneous study population, namely, a population of patients operated on for pure or predominant aortic regurgitation. They [26] tested only thromboembolism and found no independent risk factors.

Thromboembolism in our total patient population was independently related only to kidney failure, which in the coronary angiography population was related to CAD. Coronary artery disease and previous myocardial infarction were the independent risk factors in the population having coronary angiography. It has recently been shown [6] that the degree of intravascular hemolysis more than 10 years after valve replacement for AS is primarily related to impaired function of the pump, which drives the prosthesis, and only to a minor degree to the type of prosthesis. The underlying mechanism of this might also cause thrombocyte destruction and thrombus formation. Impaired left ventricular function could thus explain the adverse influence of previous myocardial infarction, which is also related to mural thrombus formation and CAD. It has been shown [27] that activated thrombocytes in patients with prosthetic heart valves play a role in thrombus formation, which is not prevented by Coumadin. Because CAD is associated with both increased platelet activation [27] and reduced thrombolytic activity [28], it is understandable that CAD increases the risk of thromboembolism.

The independent influence of previous hypertension on anticoagulant-related hemorrhage is easily comprehended, and the inclusion of increased cardiothoracic index and New York Heart Association class IV in the risk model points to the importance of end-stage AS disease. The influence of angina may be secondary to that of CAD, which is an independent risk factor in the coronary angiography group. The influence of CAD as well as of end-stage AS disease could tentatively be explained by a higher prevalence of relative liver failure, and CAD is usually also accompanied by atherosclerotic lesions of systemic arteries with a higher proneness to bleeding.

About one third of our patients who received a porcine bioprosthesis or a Lillehei-Kaster prosthesis were 45 years old or younger. The well-known accelerated degeneration rate of bioprostheses in younger patients together with the influence of small Lillehei-Kaster valves in the present study probably explains the adverse influence of age of 45 years or less on both prosthesis replacement and other prosthesis-related complications.

All prosthesis-related complications together were adversely influenced by end-stage AS disease, as exemplified by a cardiothoracic index of 0.60 or greater and an aortic valve gradient of less than 50 mm Hg (associated with narrow calcific AS and New York Heart Association class III or IV). Probably because of its influence on other prosthesis-related complications, a prosthetic valve orifice of 15 mm or less also independently increased the combined rate of complications.

Apart from emphasizing an adverse effect of the small Lillehei-Kaster valves in this study, the explanation is probably also related both to the narrow aortic root [29] and to the suboptimal hemodynamic function of small-sized Starr-Edwards [30], Björk-Shiley [29], and St. Jude valves [29, 31]. The more favorable proportion between the outer diameter of the prosthesis and the diameter of the orifice of the St. Jude valve compared with the Starr-Edwards Silastic ball valve [5] clearly favors the former in patients with a narrow aortic root.

Our 25% prevalence of Silastic ball valves with an orifice of 15 mm or less is explained by the fact that the model 1200 Silastic ball valve was the only available small prosthesis in the 1960s [31]. From the early 1970s, we preferred a disc valve for patients with a narrow aortic root. From 1980, we have used the Starr-Edwards model 1260 Silastic ball valve and the St. Jude valve almost exclusively, with a preference for the latter in a patient with a narrow aortic root and when a low profile was desirable [5]. In a comparative analysis of implantations during 1980 to 1986, the two prosthesis types performed equally well [5]. Of some importance is the finding in the present study that no patient with a Silastic ball valve experienced a thromboembolic episode after the sixth postoperative year, giving an unprecedented cumulative 15-year freedom of 90%.

The sudden cardiac-related events in our patients were most often influenced by several factors indicating a severely damaged cardiac status preoperatively. The importance of intraoperative myocardial damage is indicated by the protective influence of general hypothermia in addition to topical cooling. The influence of CAD needs no explanation. It is important to note that bypass grafting did not influence sudden cardiac-related events. We [14] have previously shown that omission of bypass grafting in patients with AS and associated CAD was an independent incremental risk factor for early mortality. The relation between ventricular ectopic beats, which also was of influence in the coronary angiography group, and advanced degrees of myocardial scarring late in the evolution of pressure-overload hypertrophy [32] plausibly explains a relation to late death from arrhythmia and to conduction block necessitating pacemaker placement.

As clearly underlined by the composition of the risk model for the combined prosthesis-related and sudden cardiac-related complications, the type of prosthetic valve was of minor importance. The present study clearly shows that by deciding on operation early in the course of AS, the cardiological-surgical team can "actively" reduce the rate of these complications. The degree of reduction that can be anticipated is indicated by the observed and predicted event-freedoms of the risk strata of the present report.

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Appendix 1. Preoperative and Intraoperative Variables Tested for Association With Prosthesis-Related and Sudden Cardiac-Related Events[a,b]

Clinical Variables

- Male sex (442)
- Age (59 ± 11 years)
- New York Heart Association functional class III (370) or IV (71)
- Dyspnea (539)
- Angina pectoris (405)
- Syncope (247)
- Previous myocardial infarction (51)
- Left ventricular failure (226)
- Right ventricular failure (144)
- Previous systemic hypertension (38)
- Digitalis and/or diuretic treatment (385)
- Antianginal and/or antiarrhythmic drug treatment (203)
- Cause
  - Degenerative/unknown (378)
  - Rheumatic (128)
  - Other (16)
- Symptom duration >60 months (168)
- Arrhythmia (23)
- Atrioventricular conduction block grades I–III (21)
- Ventricular ectopic beats (26)
- QRS duration of ≥0.12 second (51)
- ECG hypertrophy score (7.4 ± 2.6)
- Kidney failure (111)
- Cardiothoracic index (0.52 ± 0.06)
- Systemic pulse pressure (50 ± 17 mm Hg)
- Peak-to-peak systolic aortic valve gradient (95 ± 31 mm Hg)
- Left ventricular end-diastolic pressure (18 ± 10 mm Hg)
- Aortic valve regurgitation of grade 1+ or 2+ (80)
- Calcified aortic valve (613)

Operation-Related Variables

- Operative year
  - 1965–1971 (62)
  - 1972–1976 (1164)
  - 1977–1981 (158)
  - 1982–1986 (246)
- Hypothermia
  - Topical (235)
  - Topical and general (395)
- Cold blood preinfusion (458)
- Cardioplegic solution
  - Bretschneider II or III (483)
  - Bretschneider HTP (147)
- Valve substitute
  - Starr-Edwards Silastic ball (207)
  - Starr-Edwards cloth-covered (133)
  - Starr-Edwards track (146)
  - Smeloff-Cutter ball (1)
  - Lillehei-Kaster disc (25)
  - Björk-Shiley disc (10)
  - St. Jude bileaflet disc (93)
  - Porcine bioprosthesis (15)
- Prosthetic orifice diameter (17 ± 2 mm)
- Prosthetic outer diameter (25 ± 2 mm)

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[a] Data in parentheses are either the number of patients or the mean ± the standard deviation. [b] See text for definitions.

Repair of Complete Atrioventricular Septal Defect With Tetralogy of Fallot

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Repair of complete atrioventricular canal with tetralogy of Fallot was performed in 9 patients. Ventricular septal defect was closed through the right atrium using a single polytetrafluoroethylene patch with ample anterior extension to avoid subaortic obstruction. The atrial septal defect was closed with a separate patch. Undivided atrioventricular valve leaflets were sandwiched between the two patches. Right ventricular outflow tract stenosis was relieved by pulmonary valvotomy and an infundibular patch in 7, a supravalvar patch (none transannular) in 6, and right ventricle-to-pulmonary artery conduit in 2. There was one hospital death (1/9, 11%) in a patient with persistent clinically significant postoperative pulmonary stenosis and low cardiac output requiring reoperation and right ventricle-to-pulmonary artery conduit insertion. There was no late mortality. All patients are asymptomatic 0.3 to 5.6 years after operation. Follow-up right ventricular outflow tract gradient ranged from 11 to 43 mm Hg and was 70 mm Hg in 1 patient who later had successful relief of obstruction. Three patients had mitral valve insufficiency; 1 needed reoperation. Aggressive relief of right ventricular outflow tract stenosis with maintenance of pulmonary valve competence and use of two separate patches for closure of the septal defects contribute to optimum immediate and long-term results after repair of this lesion.

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Repair of isolated complete atrioventricular canal or tetralogy of Fallot can be accomplished with an acceptable mortality [1–4]. Correction of the two malformations when concurrently present is associated with unresolved surgical controversies, however, despite improved understanding of the pathology and pathophysiology of the disease [5–10]. Such controversies concern the approach for closure of the ventricular septal defect, the method of repair of the common atrioventricular valve, and the technique for relief of right ventricular outflow obstruction. We review our recent experience with surgical management of this malformation and attempt to outline certain surgical guidelines that may contribute to improved outcome.

Material and Methods

Nine patients with complete atrioventricular canal and tetralogy of Fallot underwent repair between August 1984 and September 1989. The definition of the lesion complex was based on the presence of a large nonrestrictive inlet ventricular septal defect with anterior extension, common atrioventricular valve, severe right ventricular outflow stenosis (right ventricle to pulmonary artery pressure gradient more than 40 mm Hg), and a clinically significant anterosuperior displacement of the conal septum. There were 6 female and 3 male patients. Eight patients had Down's syndrome, and 1 child had a deletion of chromosome 18. A palliative procedure in the form of a unilateral modified Blalock-Taussig shunt (4 to 6 mm in diameter) was performed in 4 patients; a bilateral shunt was performed in 2. One patient required pulmonary banding to limit pulmonary flow and control heart failure despite documented preoperative pulmonary stenosis (right ventricle to main pulmonary artery pressure gradient of 41 mm Hg). The palliative procedures were performed at between 0.1 and 3.75 years of age (mean 1.5 ± 0.9 years). Primary repair without initial palliation was accomplished in the remaining 2 patients at 1.5 and 2.1 years of age.

All patients had echocardiogram and cardiac catheterization before repair (Table 1). Nine patients had infundibular narrowing, 9 had valvar stenosis associated with annular hypoplasia (mild to moderate in 7, severe in 2), and 7 had supravalvar stenosis. The right ventricle/left ventricle pressure ratio was 1 in all patients. Pressure gradient across the right ventricular outflow tract ranged between 41 and 82 mm Hg (mean 62.6 ± 14.6 mm Hg). (Table 1). Qp/Qs ratio (after shunt operation) was 1.5/1 to 5.0/1 (mean, 2.9 ± 1.7). Two patients had moderately severe atrioventricular valve insufficiency. All patients had hypoplasia of the right ventricular outflow tract, anterior displacement of the conal septum, and moderate to severe aortic overriding (more than 50% as determined by angiographic interpretation). Seven patients had aortic–mitral valve continuity. Associated anomalies included right-sided aortic arch (2 patients) and anomalous right subclavian artery (2 patients).

Ages at repair ranged between 1.5 and 5.1 years (mean,

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Table 1. Pathology and Technique

Patient	RVOT Stenosis			RV–PA Gradient (mm Hg)	Anterior Common Leaflet Type[a]	Surgical Techniques		
	Inf	Valvar	Supravalvar			Inf Patch	Valvotomy	SV Patch
M.H.	Severe	Severe	Severe	82	A	+	+	+
D.F.	Moderate	Moderate	—	41	C	+	+	–
M.N.	Severe	Severe	Severe	57	C	+	+	+
D.L.	Severe	Severe hypoplasia	Moderate	50	C	Valved conduit 16 mm		
E.S.	Moderate	Severe annular hypoplasia	. . .	80	A	Valved conduit 18 mm		
Y.L.	Severe	Moderate	Moderate	60	C	+	+	+
M.S.	Severe	Moderate	Moderate	78	C	+	+	+
A.S.	Severe	Severe	Severe	51	C	+	+	+
J.S.	Severe	Severe	Moderate	65	C	+	+	+

[a] Rastelli classification.

Inf = infundibular; PA = pulmonary artery; RV = right ventricle; RVOT = right ventricular outflow tract; SV = supravalvar.

3.7 ± 1.2 years). At the time of operation, the ventricular septal defect involved the inlet septum and extended anteriorly in all patients. The anterior atrioventricular valve leaflet was unattached and undivided (Rastelli C) in 7 of 9 patients (77%) and divided and attached in 2 (Rastelli A) [11]. Six patients had bicuspid pulmonary valve (66%).

Surgical Technique

Surgical management of atrioventricular septal defect with tetralogy of Fallot has evolved during the past several years. Defects in all patients in this series were repaired using cardiopulmonary bypass and moderate hypothermia (25°C). Myocardial protection consisted of cold blood cardioplegia and topical cooling with ice slush. An oblique incision in the right atrial wall was made, and thorough exploration was performed. The ventricular septal defect was closed through the atriotomy using a large polytetrafluoroethylene patch fashioned like a comma or teardrop and positioned to the right of the inlet septum posteriorly and to the right of the aortic root and the conal septum anteriorly. It was secured in place with interrupted pledgetted sutures and was made wider and redundant anteriorly to accommodate any overriding of the aortic root and avoid narrowing of the subaortic area (Fig 1A–D). In 2 patients, the aortic overriding was severe, necessitating use of a small outflow ventriculotomy to complete the closure of the defect. No incision was made in the anterior or posterior leaflets of the common atrioventricular valve, and no chordal attachments of the valve to the septum were severed. The atrial septal defect was closed using a separate patch so that the atrioventricular valves were sandwiched between the atrial and ventricular patches (Fig 1E, F), and the coronary sinus was left on the right side. The mitral valve cleft was closed by approximating the anterior and posterior components of the anterior leaflet using multiple interrupted sutures placed all the way to its mural end to ensure formation of a wide leaflet. The cleft in the septal leaflet of the tricuspid valve was closed similarly. The right ventricular outflow tract was relieved by pulmonary valvotomy and infundibular resection with small right ventricular outflow patch in 7 patients. The supravalvar area was enlarged with a patch fashioned like a pantaloon and extended into the two anterior sinuses of the pulmonary valve in 6 patients. Two patients with severe hypoplasia of the pulmonary valve annulus required right ventricle to pulmonary artery valved Dacron conduits (16 and 18 mm in diameter) (Fig 1G). Transannular patching was not used.

Results

All patients were successfully weaned off cardiopulmonary bypass. Various amounts of inotropic support were required in all patients both intraoperatively and postoperatively (Table 2). All 9 patients had normal sinus rhythm. There was one hospital death in a patient who had an uneventful early postoperative course after the intracardiac repair. In the ensuing 24 hours, however, progressive right ventricular failure developed. An echocardiogram showed poor right ventricular function and a right ventricular outflow tract gradient of 36 to 40 mm Hg. The patient was reoperated on emergently with insertion of a 12-mm right ventricle to pulmonary artery valved conduit and was successfully weaned off cardiopulmonary bypass but died 12 hours later. Autopsy showed early myocardial necrosis.

Late follow-up is available on the 8 surviving patients 0.3 to 5.6 years (mean 3.5 ± 1.7 years) after operation (Table 2). There was no late mortality. All patients are asymptomatic, but 3 patients continue to receive small doses of diuretics. Right ventricle to pulmonary artery pressure gradients on follow-up Doppler echocardiograms ranged from 11 to 43 mm Hg (mean, 24.5 ± 9.8 mm

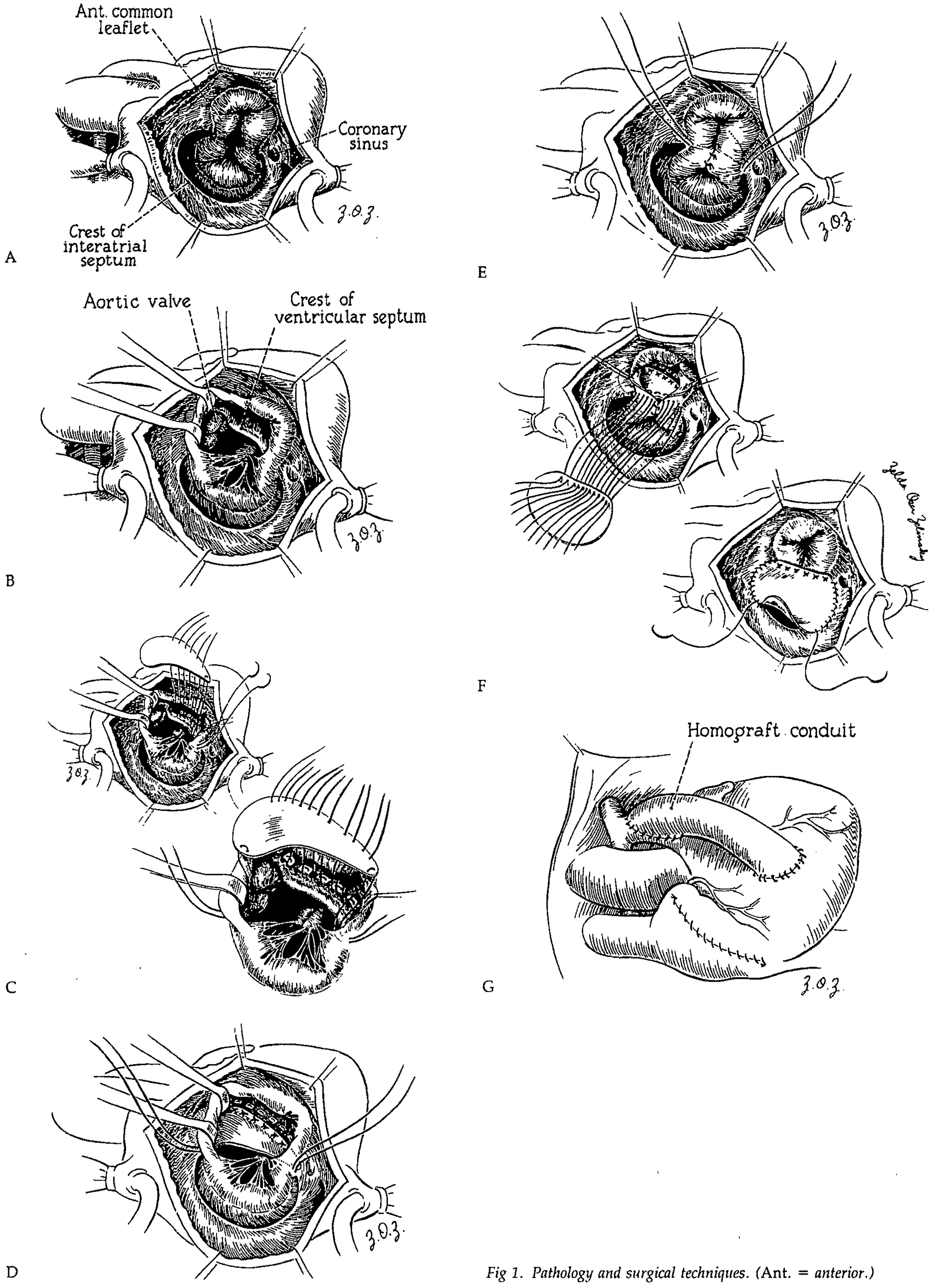

Fig 1. Pathology and surgical techniques. (Ant. = *anterior.)*

Table 2. Surgical Outcome

		Late Results				
Patient	Early Results	Duration of Follow-up (y)	RV–PA PG (mm Hg)	Residual MI	Residual TI	Present Status
M.H.	Good	3.1	70	Mild	Mild	Well; reoperated on for residual stenosis and VSD
D.F.	Good	3.4	11	Significant[a]	. . .	Well; mitral valvoplasty
M.N.	Good	5.6	20	. . .	. . .	Well
D.L.	Good	3.0	25	Trivial	. . .	Well; on diuretics
E.S.	Good	5.0	43	. . .	Mild	Well
Y.L.	Good	4.9	20	. . .	. . .	Well
M.S.	Good	0.3	28	. . .	. . .	Well; on diuretics
A.S.	Good	2.7	25	. . .	. . .	Well; on diuretics
J.S.	Poor[b]					

[a] Patient had significant preoperative atrioventricular valve insufficiency. [b] This patient had low cardiac output and residual right ventricular hypertension postoperatively and died at reoperation.

PA = pulmonary artery; PG = pressure gradient; MI = mitral insufficiency; RV = right ventricle; TI = tricuspid insufficiency; VSD = ventricular septal defect.

Hg) in 7. One patient had a progressive right ventricle to pulmonary artery pressure gradient (70 mm Hg at the time of latest cardiac catheterization). She underwent reoperation 3 years after the first operation, with patch enlargement of the right ventricular outflow tract and closure of a small residual ventricular septal defect. Two patients had mild, hemodynamically insignificant mitral regurgitation. One patient with clinically significant preoperative mitral regurgitation required reoperation and valvoplasty for residual mitral regurgitation. Two patients had mild tricuspid regurgitation. No shunts were documented by color Doppler echocardiography in any of the remaining patients.

Comment

Among the important factors contributing to successful management of patients with complete atrioventricular septal defect is postoperative competence of the atrioventricular valves [3]. Most patients have a mild degree of mitral or tricuspid valve insufficiency after repair. It is primarily owing to the morphology of the common valve and is well tolerated hemodynamically. Occasionally, serious residual mitral or tricuspid valve regurgitation persists after repair owing to defective valve tissue or faulty surgical repair and results in a serious decrease in cardiac output [6]. The presence of severe postoperative tricuspid regurgitation is particularly deleterious when complete atrioventricular septal defect is associated with tetralogy of Fallot. Under these circumstances, residual right ventricular hypertension secondary to incomplete relief of stenosis of the right ventricular outflow tract exaggerates regurgitation and impairs cardiac output, especially in the immediate postoperative period.

The surgical techniques used to repair the atrioventricular valves have varied considerably [3, 4, 12, 13]. Among the commonly used techniques is splitting of the common valve leaflets and suspension of the mitral and tricuspid components to a single patch used for closure of both the atrial and ventricular septal defects. This technique has been associated with a high incidence of serious residual mitral and tricuspid valve regurgitation owing to leaflet dehiscence or shortening [6]. In contrast, the double-patch technique used in this series secures the attachment of the valve leaflets to the neoseptum, decreases the chance of leaflet disruption, minimizes loss of valvar tissue, and produces a wider leaflet, especially when combined with aggressive closure of the valve cleft all the way to the mural side [6]. The relatively low incidence of postoperative mitral or tricuspid valve insufficiency in this series suggests that the double-patch approach is superior to single-patch closure of the atrioventricular septal defect in patients with associated tetralogy of Fallot.

Another important issue in determining the success of repair of complete atrioventricular septal defect in association with tetralogy of Fallot is the severity of the residual pulmonary stenosis and the degree of postoperative pulmonary regurgitation [6]. These lesions are relatively well tolerated in the acute postoperative period after repair of isolated tetralogy of Fallot, although at the expense of progressive right ventricular dysfunction later [14, 15]. In the presence of tricuspid regurgitation after atrioventricular valve reconstruction, however, clinically significant obstruction of the right ventricular outflow tract or volume overload from pulmonary insufficiency is not as well tolerated [4, 5]. Ideally, therefore, the obstruction of right ventricular outflow tract in this complex is best relieved by resecting the obstructive muscles through the tricuspid valve to avoid a right ventriculotomy with its attendant ventricular dysfunction by performing a pulmonary valvotomy and by patching the supravalvar pulmonary artery [10]. In patients with severe infundibular hypoplasia and substantial anterior displacement of the conal septum, an additional patching of the outflow tract of the right ventricle may be required. The presence of clinically significant pulmonary valve annular hypoplasia and stenosis, often treated by use of a transannular patch, should preferably be relieved by insertion of a right ventricle to pulmonary artery valved conduit to bypass the obstruction without producing pulmonary valve insufficiency. Although Urotzky and colleagues [12] and Vargas and co-workers [6] reported no side effects from use of the transannular patch, our experience and that of other investigators suggests that pulmonary regurgitation is not well tolerated in this group of patients, primarily in the early postoperative period when valve competence is necessary to achieve hemodynamic stability [4]. Our data suggest that use of a valved conduit is to be recommended if preoperative assessment of the hypoplastic pulmonary valve annulus predicts a postoperative pressure gradient across the right ventricular outflow tract of 40 to 50 mm Hg or more [2]. The only disadvantage of this approach for relief of outflow obstruction is the need for subsequent conduit change because of progressive stenosis. This might not be necessary for all conduits, however, because the outflow tract and the valve annulus could enlarge after repair, obviating the need for future conduit replacement. Use of a transannular patch with a monocusp is an attractive alternative to conduit insertion, but it was not used in this series.

Subaortic stenosis could complicate intracardiac repair of this anatomical complex [12]. The ventricular septal defect extends anteriorly and is associated with serious overriding of the aorta in most patients. Some investigators [4, 7] have suggested the use of two patches, one posterior and the other anterior, to close the ventricular septal defect without narrowing the left ventricular outflow tract. This necessitates a large right ventriculotomy to insert the patch around the anterior portion of the defect and the aortic root and may result in ventricular dysfunction. Other investigators [6] have recommended splitting the anterior common atrioventricular valve leaflet to the right of the septum to allow more space for the ventricular patch and to prevent narrowing of the outflow tract of the left ventricle. We have found that the defect can be closed by using the right atrial approach in most patients, thus limiting the length of the right ventriculotomy, if any, to the minimum necessary to achieve relief of the right ventricular outflow obstruction [12]. Such an approach is made particularly easy in this lesion because of the frequent presence of a free floating (not attached to the septum) common anterior leaflet, facilitating retraction of the atrioventricular valve and visualization of the anterior portion of the aortic root from the right atrium. Tailoring the patch to be wide and redundant anteriorly in the shape of a comma or teardrop provides ample enlargement of the left ventricular outflow tract and eliminates subaortic obstruction. When a right ventricular to pulmonary artery conduit is needed, the anterior portion of the ventricular septal defect may be closed through the ventriculotomy, using an additional patch around the aortic root to enlarge that area. In an occasional patient, the aortic overriding may be so severe that it results in a decreased clearance between the crest of the ventricular septum and the atrioventricular valve, a potential source of subaortic stenosis. Enlargement of the anterior portion of the ventricular septal defect may be necessary to eliminate such a possibility.

When feasible, it is preferable to perform primary complete repair rather than initial palliation in patients with atrioventricular septal defects associated with tetralogy of Fallot [16]. This is best achieved when the patient is aged 1 year or more. Very young patients or patients with hypoplastic pulmonary artery or pulmonary valve annulus require palliation with a modified Blalock-Taussig shunt. Delaying correction beyond age 1 year provides several advantages. The atrioventricular valve leaflets usually thicken with time, making valve reconstruction easier and more durable. More complete relief of right ventricular outflow obstruction is likely to be achieved without the need for enlarging the pulmonary valve annulus, which is frequently very hypoplastic in younger patients. Moreover, a larger conduit could be inserted in older patients if such a need arises. These advantages outweigh the potential risks of temporarily keeping the heart subject to chronic volume and pressure overload until the lesion ultimately is repaired.

Although the mortality rate in this series is quite favorable, future decrease in perioperative complications is expected. Use of fresh homografts to bypass right ventricular outflow obstruction could provide an additional thrust toward achieving the best possible surgical results in patients with the combination of tetralogy of Fallot and atrioventricular septal defect.

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REVIEW OF RECENT BOOKS

Atlas of Cardiothoracic Surgery
By L. H. Edmunds, Jr, W. I. Norwood, and D. W. Low
Philadelphia, Lea & Febiger, 1990
287 pp, illustrated, $125.00

Reviewed by Riyad Y. Tarazi, MD

The *Atlas of Cardiothoracic Surgery* by Edmunds, Norwood, and Low covers cardiac and thoracic surgery as practiced in the 1990s in a simple and explicit way. This atlas can be used as a quick reference by practicing surgeons, residents, students, and health-care professionals. Although no atlas can cover in detail all modifications of technique practiced, this one comes as close to that as possible. The sections on acquired and congenital heart disease, pulmonic disease, and esophageal disease are complete. I believe that this book is a valuable addition to one's library.

San Diego, California

Arteriosclerosis of the Gastroepiploic and Internal Thoracic Arteries

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Arteriosclerosis of the right gastroepiploic artery (GEA) and the internal thoracic artery (ITA) were compared by pathological observation. Specimens were obtained from 35 patients who underwent coronary artery bypass grafting with simultaneous use of these two kinds of arterial grafts. Degree of arteriosclerosis was classified in five categories: 0, normal; 1, luminal narrowing less than 25%; 2, luminal narrowing between 25% and 50%; 3, luminal narrowing greater than 50%; and 4, overt atherosclerosis with ulceration or calcification. The number of arteries with degree 0, 1, 2, 3, and 4 was 16 (46%), 15 (43%), 3 (9%), 0, and 1 (3%) in GEA and 27 (77%), 8 (23%), 0, 0, and 0 in ITA, respectively. Incidence of degree 0 was higher in ITA, but differences were not significant. The mean wall thickness was 0.30 ± 0.13 mm in GEA and 0.21 ± 0.07 mm in ITA ($p < 0.05$). In 23 patients who underwent postoperative angiography, all 46 arterial grafts were patent without focal stenosis. We conclude that GEA has slightly more intimal thickening than ITA, but significant luminal narrowing caused by arteriosclerosis is rare. Gastroepiploic artery can be expected to be a suitable conduit for coronary artery bypass grafting.

(Ann Thorac Surg 1990;50:413–6)

The right gastroepiploic artery (GEA) has recently become recognized as a suitable conduit for coronary artery bypass grafting (CABG) because of its similarity in size to the coronary artery, the technical feasibility of in situ grafting, and the lack of gastric complications after division of the GEA [1–5]. The incidence of arteriosclerosis of GEA has not been widely investigated, however. Larsen and colleagues [6] described the incidence of arteriosclerosis of the gastroduodenal artery and the other abdominal arteries in comparison with the coronary artery. In the present study, we made a pathological comparison in the clinical setting between the GEA and the ITA, which is already known to have relative immunity from atherosclerosis.

Material and Methods

Specimens of GEA and ITA were taken from 35 patients who underwent CABG with combined arterial grafts. After harvesting these two kinds of arteries by a technique previously described [2], we obtained materials just distal to the anastomotic site of each artery without any mechanical dilatation. Pathological observation was made under hematoxylin-eosin and elastica van Gieson staining.

Subjects were 29 Japanese men and 6 Japanese women ranging in age from 45 to 72 years (mean age, 58.4 years). All patients had severe stenoses in all three major coronary artery branches except for 3 patients with double-vessel disease. Eleven patients had hypertension, 10 patients had diabetes mellitus (3 required insulin), and 9 patients had hypercholesterolemia (more than 5.95 mmol/L [230 mg/dL]). Severe occlusive disease in the aortoiliac artery was associated in 3 patients, and palpable atherosclerotic lesion in the ascending aorta was noted in 4 patients.

The degree of arteriosclerosis was classified in five categories: 0, normal; 1, intimal thickening of the thickest part occupying less than 25% of the luminal diameter; 2, intimal thickening occupying between 25% and 50% of the luminal diameter; 3, intimal thickening occupying more than 50% of the luminal diameter; and 4, apparent atherosclerotic change with ulceration or calcification (Table 1). Wall thickness of specimens was also measured.

In 23 patients, postoperative angiography was performed within 6 postoperative months. Student's t test and χ^2 test were used for statistical analysis.

Results

The number of arteries with degree 0, 1, 2, 3, and 4 was 16 (46%), 15 (43%), 3 (9%), 0, and 1 (3%) in GEA and 27 (77%), 8 (23%), 0, 0, and 0 in ITA, respectively (Table 1). The incidence of degree 0 was higher in ITA, but differences were not significant. One GEA with degree 4 was not discarded, but was used to bypass the right coronary artery because its free flow was good (160 mL/min) after additional excision of the distal end. Because this patient had severe occlusive disease in bilateral iliac arteries, postoperative celiac angiography could not be performed. No signs of myocardial ischemia and chest pain have been noted in this patient. The wall thickness of GEA was 0.30 ± 0.13 mm (range, 0.1 to 0.7 mm), which was significantly thicker ($p < 0.05$) than that of ITA, which had a mean of 0.21 ± 0.07 mm (range, 0.1 to 0.3 mm). Typical histological views of GEA are shown in Figure 1. Figure 2 shows the histology of GEA and ITA of degree 0 as well as

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Table 1. Grading of Arteriosclerosis of the Gastroepiploic Artery and the Internal Thoracic Artery

Degree	Definition	GEA (n = 35)	ITA (n = 35)	*p* Value
0	Normal	16 (46%)	27 (77%)	NS
1	Less than 25% narrowing	15 (43%)	8 (23%)	NS
2	25% to 50% narrowing	3 (9%)	0	NS
3	More than 50% narrowing	0	0	NS
4	Calcification	1 (3%)	0	NS

GEA = gastroepiploic artery; ITA = internal thoracic artery; NS = not significant.

postoperative angiograms of those grafts in a 61-year-old man.

The amount of elastic tissue in the media was apparently higher in ITA than in GEA in most patients (Fig 3). All 23 grafts of GEA and ITA were patent at postoperative angiography. Two of these GEAs were opacified through the superior mesenteric arteriography. No segmental stenosis was found in the trunk of any GEA or ITA graft.

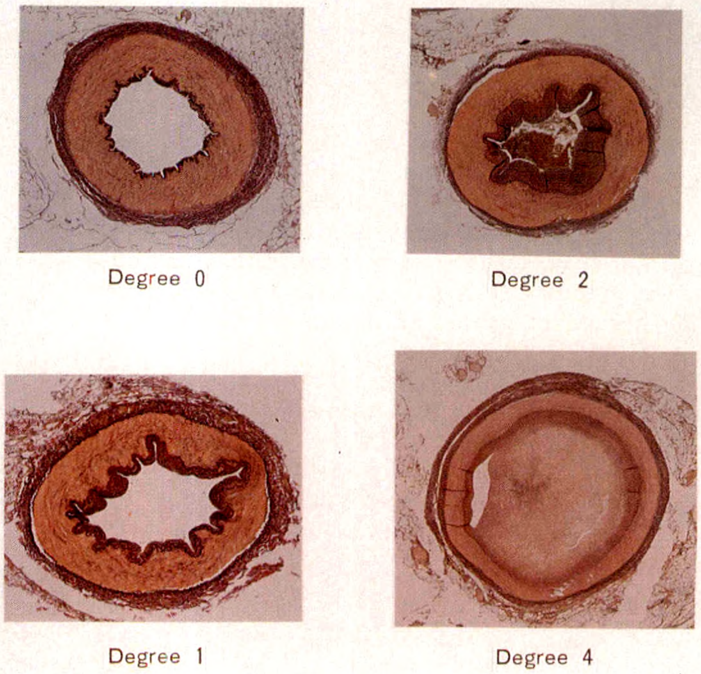
Comment

Successful clinical reports of the GEA graft in CABG were described by Pym and colleagues [1] and Suma and co-workers [7] in 1987. Its clinical application is increasing [2–5]. Numerous experiences show that GEA has a diameter similar to that of the coronary artery and a proper length to be used as an in situ graft; it poses no gastric complications related to devascularization and has an adequate flow capacity. To predict its long-term patency, which is still unknown, the incidence and grade of arteriosclerosis of GEA should be clarified.

In 1969, Larsen and colleagues [6] studied the incidence of arteriosclerosis in various sites of human arteries in elderly patients at autopsy. They reported that the gastroduodenal artery, the upstream of the GEA branched from the common hepatic artery, apparently has less arteriosclerosis than the coronary artery. They graded arteriosclerotic changes in four degrees as we did, and the number of vessels in grade 1 to 4 (from normal to severely diseased) was 37 (36%), 58 (57%), 2 (2%), and 5 (5%) in 102 gastroduodenal arteries and 0, 14 (14%), 33 (32%), and 56 (54%) in 103 coronary arteries. In our study, we compared arteriosclerotic changes between GEA and ITA obtained from surgical specimens in patients with significant arteriosclerosis in their coronary arteries and some other sites, such as the ascending aorta or the femoral artery. Even in these highly arteriosclerotic patients, most ITAs were free of arteriosclerosis as previously reported [8–10]. On the other hand, GEA showed a higher incidence of mild intimal thickening (degree 1) than did ITA; 31 of 35 GEAs (89%) had a clinically normal appearance, however (degree 0 and 1). Only one GEA showed overt atherosclerosis (in a patient with associated aortoiliac occlusive disease). Elastic tissue was rich in the media of ITA in many cases, but was rare in GEA, as Mills and Everson reported [4]. The wall was thicker in GEA (0.30 mm) than in ITA (0.21 mm) in many instances, which was advantageous in the operating room because a thicker wall makes suture of GEA easier.

Although other important anatomical factors such as integrity of the internal elastic lamina [11] or the relationship between the vessel wall thickness and the vasa

Fig 1. Microscopic views of the gastroepiploic artery: normal (left, top), mild (left, bottom), moderate (right, top), and severe (right, bottom) arteriosclerotic changes. (Elastica van Gieson, ×20 before 16% reduction.)



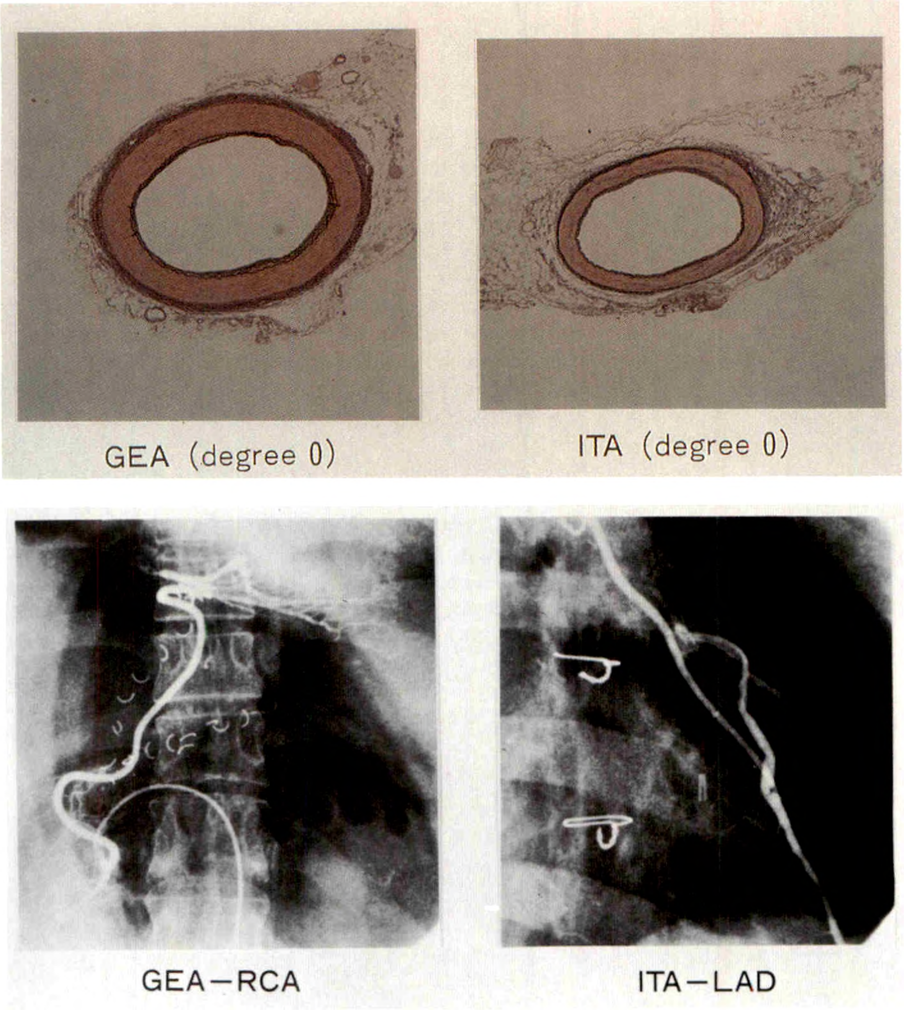


Fig 2. Histology (top) and postoperative angiograms (bottom) of gastroepiploic artery (GEA) and internal thoracic artery (ITA) grafts in a 62-year-old man. (Elastica van Gieson, ×20 before 31% reduction.) (LAD = *left anterior descending coronary artery;* RCA = *right coronary artery.)*

vasorum [12] must be considered with regard to the patency of the autologous graft, they were not investigated in this study. Biochemical factors such as prostacyclin [13], endothelium-derived relaxing factor [14], and other endothelial substances may also play some role in graft patency. Therefore, the grade of arteriosclerosis of autologous arterial graft is not the single determinant factor for long-term patency of the graft. We believe, however, that a mild degree of arteriosclerosis in GEA, although slightly greater than in ITA, is strong supportive

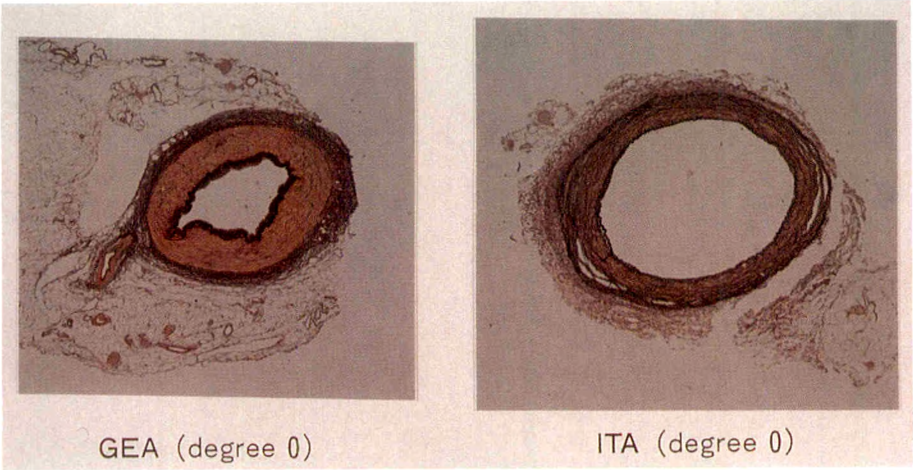


Fig 3. Histology of the gastroepiploic artery (GEA) and the internal thoracic artery (ITA) in a 60-year-old man. Elastic tissues in the media (stained black) are apparently rich in the ITA, whereas they are quite rare in the GEA. (Elastica van Gieson, ×20 before 30% reduction.)

evidence that GEA will have good long-term patency as a coronary artery bypass graft.

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Superior Vena Caval Reconstruction Using Autologous Pericardium

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Tumor involvement of the superior vena cava can occur either by direct extension of the primary tumor or by invasion of superior mediastinal lymph nodes. Removal of a portion of the caval wall may be required to allow adequate margins of resection. The technique described involves placement of an intraluminal shunt and resection of the involved caval wall with reconstruction using autologous pericardium.

(Ann Thorac Surg 1990;50:417–9)

Bronchogenic carcinoma can involve the superior vena cava either by direct extension of the primary tumor or by invasion of superior mediastinal lymph nodes. A complete and margin-free resection may require removal of a portion of the wall of the superior vena cava or innominate vein.

Reports have described bypassing or replacing an obstructed superior vena cava secondary to tumor involvement with a variety of materials, including Dacron (C.R. Bard, Billerica, MA), Gore-Tex (W.L. Gore, Elkton, MD), saphenous vein, and pericardium [1–4]. When an obstructed superior vena cava is bypassed, the construction of a temporary shunt is usually not required as adequate collateral pathways have already developed. In contrast, clamping and reconstruction of a nonobstructed superior vena cava can result in hemodynamic compromise intraoperatively owing to an abrupt decrease in venous return to the heart during clamping. A sudden increase in intracranial venous pressure may also cause irreversible brain damage, and the possibility of an intracranial bleeding episode exists [5, 6]. For these reasons, we have always shunted blood from the innominate vein to the right atrium during resection of a nonobstructed superior vena cava. This technique involves placing a tube through the right atrium into the right innominate vein, and, in our experience, has been simple to perform and successful.

Operative Technique

If the tumor of the lung is large and bulky and there is direct extension into the wall of the vena cava, the technique of vena caval shunting and resection of a portion of its wall can be more easily accomplished if the lung has been removed. In this instance, it may be necessary to cut through the tumor just distal to the involvement of the wall of the vena cava. Seeding of the operating field by tumor cells is speculative, but the added exposure for shunting, resection, and reconstruction has been of benefit. This is not required when lymph nodes invade the wall of the vena cava as an en-bloc resection can be performed. The pericardium is opened as close to the hilum as possible in an attempt to avoid prosthetic patch repair of a large pericardial defect, but the opening must be generous enough to provide adequate exposure of the atrium and proximal cava. If the phrenic nerve has not been involved by the tumor, it can be dissected free and retracted medially.

A careful and complete dissection is required to expose adequate lengths of both the right and left innominate veins. Umbilical tapes are then placed around the cava at the atriocaval junction and around each individual innominate vein. The tourniquet at the atriocaval junction should be positioned slightly above the actual junction, if the tumor margin permits, to avoid potential injury to the sinoatrial node. We have not experienced any rhythm disturbances with this technique.

The azygos vein is routinely ligated if it has not previously been thrombosed by tumor. A 20F thoracostomy tube is then prepared to serve as the shunt. The distal end of the tube must be cut off so that only two or three sideholes of the chest tube remain and are distal to the occluding tourniquet at the innominate level. The tube is then measured against the length of the superior vena cava and right atrium, and a single hole is cut into the side wall of the tube at an appropriate distance that will permit the side hole to direct the flow of shunted blood into the right atrium and still be distal to the occluding atriocaval tourniquet.

The patient is then anticoagulated with 5,000 U of sodium heparin given intravenously. A pursestring suture is placed in the wall of the right atrium just as if one were preparing the placement of a venous drainage catheter for cardiopulmonary bypass. A stab wound is made into the atrium wall in the center of the pursestring suture, and the shunt is inserted into the right atrium and through the vena cava into the right innominate vein. The distal end of the shunt is occluded with a clamp. Securing the tourniquets with careful positioning of the shunt will effectively isolate the involved portion of the superior vena cava while maintaining venous return to the heart (Fig 1A). The involved caval wall can then be completely resected with histological examination of the margin by frozen-section analysis. We have usually been able to

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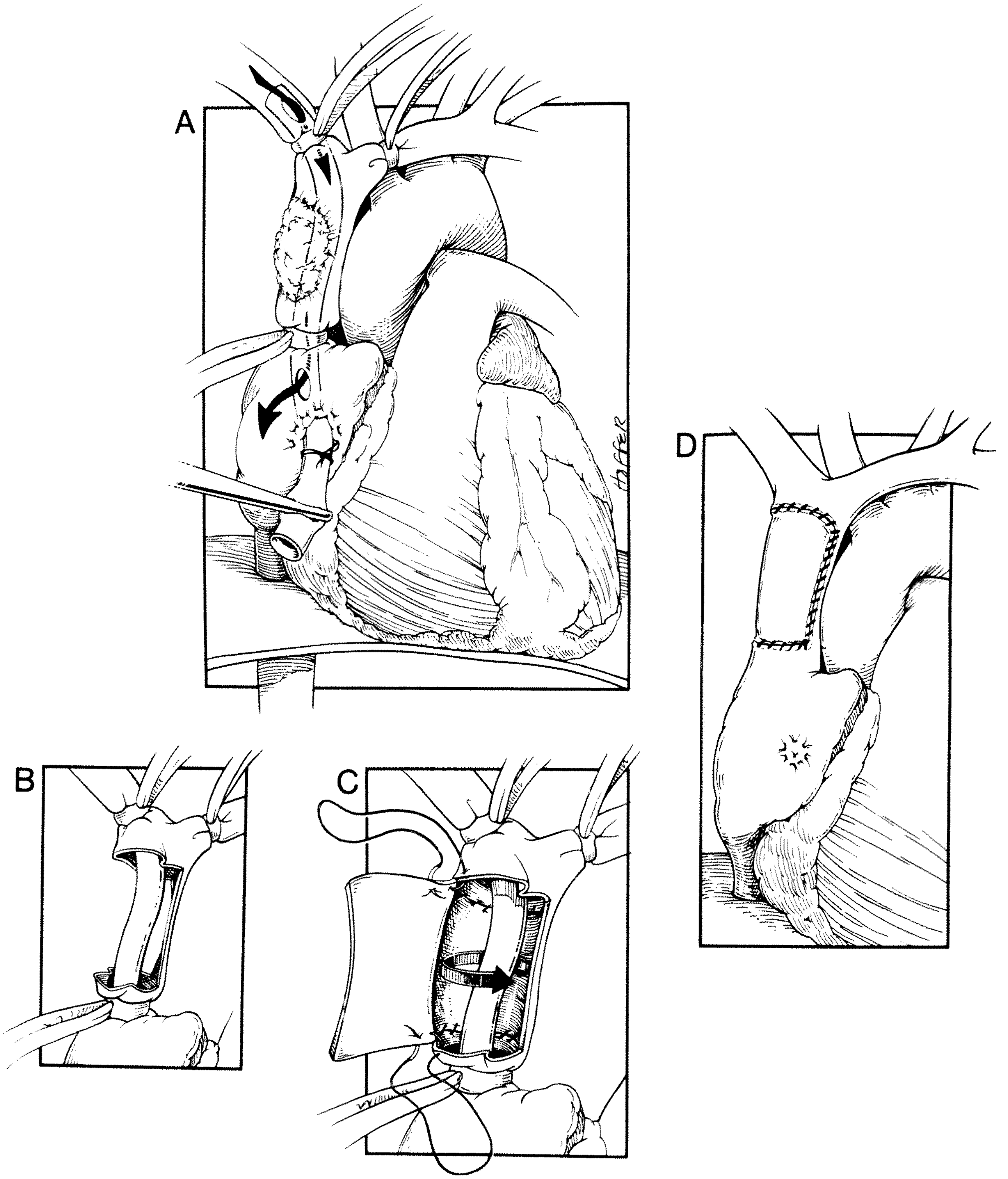

Fig 1. (A) Shunt properly positioned in the superior vena cava by right atrial pursestring. (B) Tourniquets snared to allow isolation and excision of involved caval wall. (C) Pericardial flap sutured into place. Suture line should begin on the most posterior and medial aspect of the caval wall. (D) Completed reconstruction with shunt removed and flow reestablished.

retain a segment of the medial vena cava in our resections (Fig 1B).

We do not routinely use a central venous pressure catheter as it would lie in the area of caval resection; however, the anesthesiologist is alerted to watch the face and neck veins carefully for engorgement while the shunt is in place. The flow through a 20F catheter has been adequate in our experience to date.

Table 1. Summary of Patients Undergoing Concomitant Superior Vena Caval Reconstruction and Pulmonary Resection[a]

Sex	Age (y)	Operation	SVC Specimen	Follow-up
M	60	Right pneumonectomy, squamous cell CA	Positive	DOD at 11 mo, SVC patent at autopsy
M	40	Right upper lobectomy, neuroendocrine CA	Positive	NED at 42 mo
F	42	Right pneumonectomy, squamous cell CA	Positive	DOD at 4 mo
F	73	Right pneumonectomy, squamous cell CA	Positive	Dead of arrhythmia at 17 days, SVC patent at autopsy
M	52	Right sleeve pneumonectomy, squamous cell CA	Positive	NED at 14 mo
M	61	Right pneumonectomy, neuroendocrine CA	Positive	NED at 4 mo

[a] Margins of resection at operation were free of tumor in all patients.

CA = carcinoma; DOD = dead of disease; NED = no evidence of recurrent disease; SVC = superior vena cava.

A piece of pericardium large enough for reconstruction of the caval defect is then obtained. The pericardium is sutured into the caval defect with a running 4-0 Prolene suture (Ethicon, Somerville, NJ) beginning posteriorly and medially (Fig 1C). The pericardium is oriented with the visceral surface toward the caval lumen. The sutures should be closely spaced, and the patch is always made patulous to avoid any possibility of lumen compromise. Once the procedure is completed, the innominate tourniquets are released to aid in removal of air before removal of the shunt (Fig 1D).

It is always necessary to evaluate carefully the size of the resulting pericardial defect to judge whether cardiac herniation may occur. It may be necessary to place a prosthetic patch to avoid this complication, particularly if a right pneumonectomy has been accomplished.

Comment

We used this technique of superior vena caval shunting, resection, and reconstruction in 6 patients with caval wall involvement with tumor and achieved satisfactory results (Table 1). One patient died in the early postoperative period of a ventricular arrhythmia; postmortem examination showed a patent superior vena caval reconstruction without evidence of stenosis or thrombus. A second patient died of recurrent disease at 11 months, and again postmortem examination showed a patent reconstructed vena cava. The remaining patients have not had clinical evidence of caval obstruction or any complications related to this technique. Assessment of patency has been made only by clinical examination to date. We do not believe that use of more invasive methods of assessment are justified in this population of patients with advanced disease.

We favor the use of pericardium over prosthetic materials such as Gore-Tex or Dacron primarily because of the potential of thrombogenicity. Spiral saphenous vein grafts potentially could be used for this application but we find them to be more time consuming without any obvious advantage.

This technique has not been used in superior vena cavas that are totally obstructed by tumor, and we do not advocate the described technique for that application. However, this technique can be of benefit when resection of a large portion of the superior vena cava is necessary to achieve a complete resection. Experience to date is still too limited to assess accurately any impact on patient survival using this technique with concomitant pulmonary resection for bronchogenic carcinoma.

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Use of Pedicled Omental Flap in Treatment of Empyema

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Omental pedicle flaps were used in the treatment of patients with acute and chronic empyema with bronchopleural fistula. In 5 patients (group 1) with postoperative acute empyema owing to bronchial stump fistula, an omental covering was applied as a reinforcement to close the fistula. Six patients in group 2 with chronic tuberculous or *Aspergillus* empyema with multiple fistulas initially underwent open-window thoracostomy or cavernostomy and secondarily had omental transposition. In all patients, the right gastroepiploic vessels were used to provide the blood supply for the flap. Successful closure of the bronchial stump was obtained in all patients in group 1, but 2 of them died of recurrence of their underlying lung carcinoma within 1 year. Five of the 7 patients in group 2 had a favorable outcome, but 2 patients had partial recurrence after omental plombage. From our experience with these patients, we believe that the omental flap is effective for closing fistulas due to postoperative or chronic empyema but has only limited success in patients whose lungs are severely damaged by persistent infection.

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Treatment of acute and chronic empyema, including postlobectomy empyema, postpneumonectomy empyema, and tuberculous or nontuberculous empyema, has been a major concern of thoracic surgeons [1–4]. Despite the decreasing use of resection as a treatment method for intrapulmonary tuberculosis, chronic tuberculous empyema must often be treated surgically. Although several operative procedures have been developed with varying degrees of success [1–3, 5–8], the method of treating empyema, and in particular empyema associated with fistula, remains controversial.

The omentum has been used for management of complicated problems in various fields of general surgery and cardiovascular surgery [9–18]. It has also been used in repair or reconstruction of organs with ischemic damage and as an aid in the healing or closing of various types of fistulas [7, 10, 12, 16]. Some successful results have been achieved by use of the omentum in patients with thoracic empyema resulting from bronchial fistula [7, 16]. We have performed operations using the omentum in 12 patients with acute and chronic empyema and achieved favorable results in 10. We report our series of patients and discuss the value of the omental flap in the surgical treatment of thoracic empyema, its indications, and its limitations.

Material and Methods

Since January 1980, 12 patients have undergone omental transposition in our departments. The 9 men and 3 women were divided into two groups (Tables 1, 2). Group 1 consisted of 5 patients who had postoperative acute empyema (4 had postpneumonectomy empyema, and 1 had empyema after right middle and lower lobectomy). The 7 patients in group 2 had chronic empyema: 5 had tuberculous empyema, and 2 had *Aspergillus* empyema. The underlying disease of the 5 patients in group 1 was lung carcinoma (see Table 2). Chronic empyema due to tuberculous or aspergillosis in group 2 was discovered after the development of symptoms related to bronchopleural fistulas.

A single-stage operation was performed in all patients in group 1 and in 1 patient in group 2. Two-stage procedures (open-window thoracostomy or cavernostomy and then omental plombage) were performed in the remaining 6 patients with chronic empyema (see Tables 1, 2). In these patients, two or three segments of rib were resected and the empyema space was fully exposed at the initial operation. Postoperatively, daily gauze dressings were applied until fresh granulations appeared in the open space (a period of 1 to 9 months). Omental plombage was performed as a secondary procedure. *Staphylococcus aureus* was detected in the empyema space in 6 patients with postpneumonectomy empyema. In the chronic empyema group, only 1 patient (patient 8) was positive for tuberculous bacilli, whereas *Aspergillus* was demonstrated in 2 patients by culture. Tuberculous or mycotic lesions were histologically confirmed in all resected specimens in group 2.

For transposition of the omentum, a short median incision was made in the upper abdomen and the greater omentum was freed from the greater curvature of the stomach proceeding from left to right. In all patients, the

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Table 1. Patients With Postoperative Empyema Who Underwent Omental Transposition (Group 1)

Patient No.	Sex	Age (y)	Underlying Disease	Type of Fistula	Operation	Outcome
1	M	71	Right lung carcinoma	Bronchial stump fistula after pneumonectomy	TD, OC	Successful closure; died after 3 mo of tumor recurrence
2	M	52	Right lung carcinoma	Bronchial stump fistula after pneumonectomy	TD, OC	Successful closure; died after 1 y of tumor recurrence
3	M	56	Right lung carcinoma	Bronchial stump fistula after middle and lower lobectomy	TD, OC	Successful closure; alive 1 y 3 mo postop
4	M	63	Right lung carcinoma	Bronchial stump fistula after pneumonectomy	TD, carinal resection and OC	Successful closure; alive 1 y 3 mo postop
5	M	56	Right lung carcinoma	Bronchial stump fistula after pneumonectomy	TD, OC	Successful closure; alive 1 y 3 mo postop

OC = omental covering; Successful closure = successful closure of bronchial fistula; TD = tube drainage.

omental flap was supplied by the right gastroepiploic vessels. A hole admitting two or three fingers was made in the diaphragm below the sternum, and the omental flap was generally brought up into the lower thoracic space without difficulty through this hole. In the patients with chronic empyema in the upper thorax (patients 9 and 10, Table 2), however, intrathoracic transfer of the omentum was difficult because the adhesions between lung and chest wall or diaphragm were very firm. In those patients, we made a subcutaneous tunnel and passed the omentum through it to bring it up into the empyema space (Fig 1).

For closure of the fistulas in most patients in group 2, we sutured individual fistulas except for the smallest ones, which were left to close spontaneously. In patient 8, in whom the dissection and suturing of a larger fistula proved difficult, we pushed a part of the omentum into the fistula while covering the lung with omentum. In all patients, the omental flap was fixed to the bronchial wall with Dexon sutures, and fibrin glue was poured into the space around the omentum. In 4 patients with chronic empyema, we performed additional plombage using the surrounding chest wall muscles (pectoralis major and serratus anterior muscles for anterior lesions and latissimus dorsi for posterior lesions), because in those patients

Table 2. Patients With Chronic Empyema Who Underwent Omental Plombage (Group 2)

Patient No.	Sex	Age (y)	Cause of Empyema	Location of Empyema in Thoracic Space	Operation	Outcome
6	F	65	Tuberculous empyema with fistulas	Right lower	OWT, decortication, and omental transposition	No recurrence at 3 y 5 mo; alive and well
7	F	32	*Aspergillus* empyema with fistulas	Right upper	OWT, omental transposition	No recurrence at 2 y 9 mo; alive and well
8	M	74	Tuberculous empyema with fistulas	Left lower	OWT, omental transposition, and muscle plombage	Partial recurrence at 2 y 5 mo; alive
9	M	68	Tuberculous empyema with fistulas	Right upper	OWT, omental transposition, and muscle plombage	Partial recurrence at 2 y 5 mo; alive
10	M	76	*Aspergillus* empyema with fistulas	Left upper	Open-window cavernostomy, omental and muscle plombage	Partial recurrence at 2 y 2 mo; alive
11	F	66	Tuberculous empyema with fistulas	Right lower	OWT, omental transposition, and muscle plombage	6 mo postop
12	M	72	Tuberculous empyema with fistulas	Right total	OWT, omental transposition	6 mo postop

OWT = open-window thoracostomy.

the omentum was of insufficient volume to cover the entire surface of the damaged lung.

In patients with postoperative bronchial stump fistulas, tube drainage and irrigation was performed initially. Next, the pleural space was opened and the entire surface of the empyema cavity was irrigated thoroughly. After exposing healthier tissue belonging to the bronchial stump as far as possible, we performed repeat resection and closed the stump. Finally, we bunched the transferred omentum and sutured it to the bronchial stump in some areas.

Results

We obtained favorable postoperative results in 5 patients in group 2 with chronic empyema (patients 6, 7, 8, 11, and 12); 2 had partial recurrence (patients 9 and 10) (see Table 2). Patient 6 had a right chronic empyema with fistulas. Long-term management with tube drainage was a failure, but omental transposition was subsequently performed successfully (Fig 2). Patient 7 was a very short and thin woman. She had undergone long-term medical therapy for pulmonary tuberculosis, but an intracavitary aspergilloma subsequently developed. An open-window cavernostomy was performed. At the closure of this large open space, sufficient chest wall muscle was not available for plombage; therefore, only the omentum was placed over the openings of the fistulas. Postoperatively, the dead space slowly decreased with time (Figs 3 and 4). Patients 6 and 12 also did not undergo additional plombage using chest wall muscles.

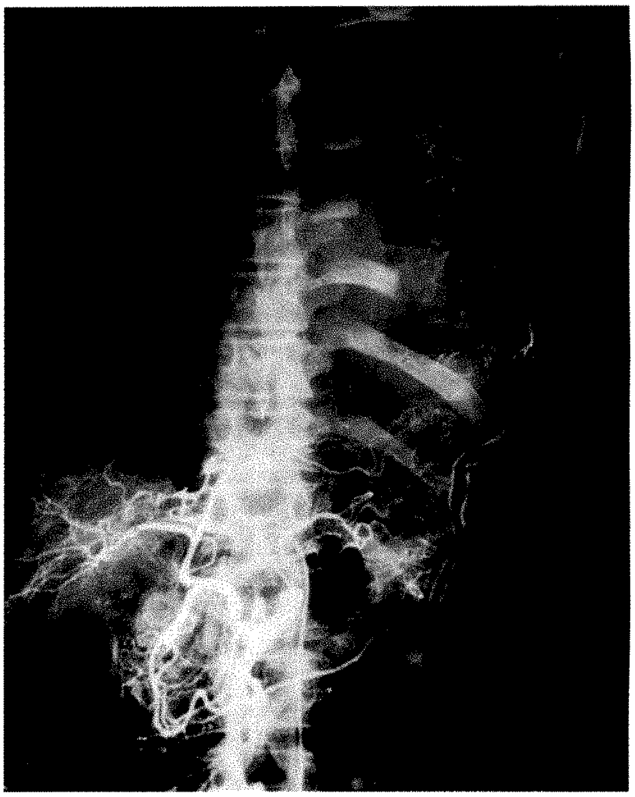

Fig 2. A celiac angiogram performed 3 months after omental transposition in patient 6 shows the patency of the right gastroepiploic vessels that run into the left thorax.

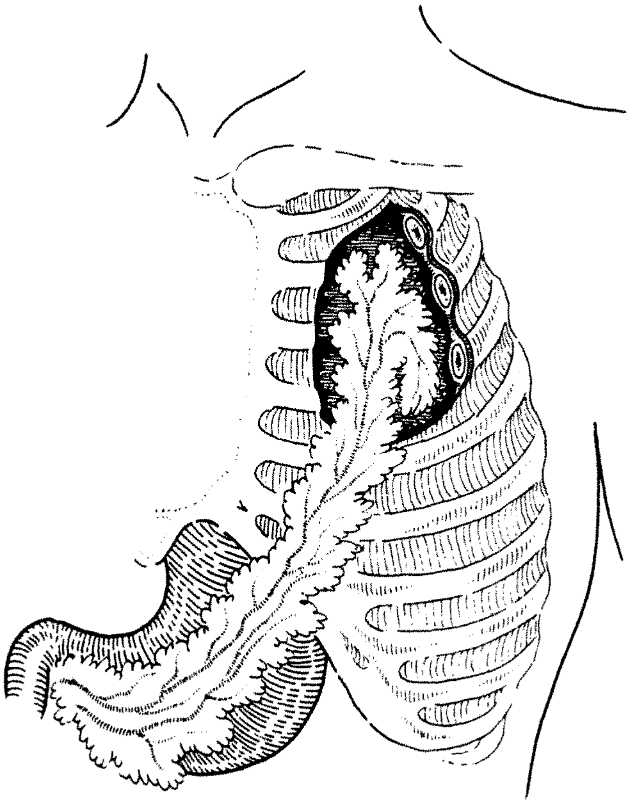

Fig 1. Method of transposing the omentum in a patient whose empyema space is located in the upper thorax and whose residual lung has tight adhesions to the thoracic wall. The omentum is brought up through a subcutaneous tunnel.

In patients with successful results, pulmonary symptoms resolved completely and there has been no recurrence during follow-up. Patients 9 and 10 had recurrence of symptoms about 1 month after omental plombage. Both of them were malnourished elderly patients with large empyemas and persistent infection of the lung parenchyma in whom pleuropneumonectomy was impossible because of their poor general condition and reduced lung function. In patient 9, after an open-window thoracostomy, the omentum and chest wall muscles were used to cover many fistulas of various sizes. Postoperative bronchography showed, however, that obliteration of the fistulas was only partially successful. In patient 10 a recurrent free space developed 1 month after operation and repeat cavernostomy showed partial recurrence of the fistulas even though the omentum was viable and tightly adherent to the top of the empyema space. Patients 11 and 12 are alive and well 6 months after operation, but it is too early to assess the long-term results in these patients.

In all patients with postoperative acute empyema (group 1), we successfully achieved closure of the bronchial fistula by using the omental covering (Table 1). Four of the 5 patients in this group had stage III lung carci-

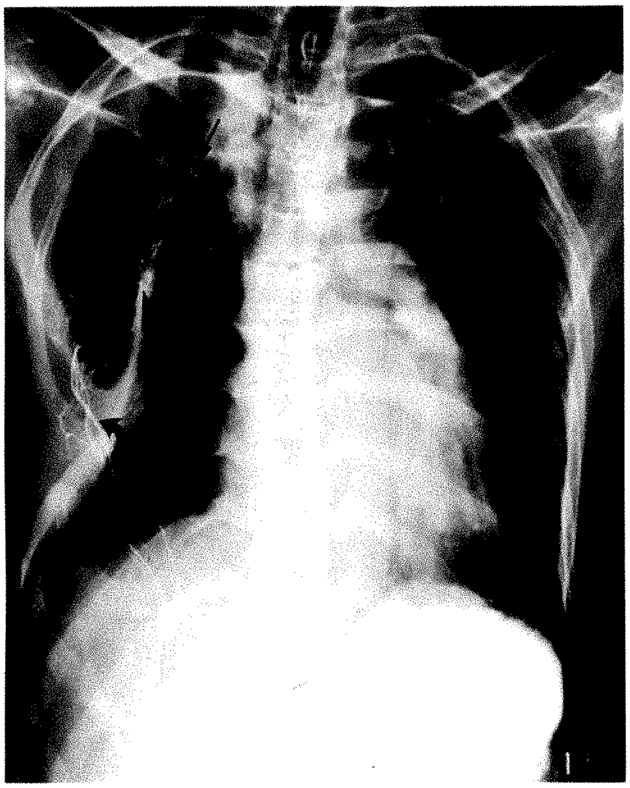

*Fig 3. A celiac angiogram performed 3 weeks after omental transposition in patient 4 shows thin omental vessels (*arrows*) covering the surface of the bed of a large empyema space.*

noma, and 1 had a stage I tumor. Patient 1 died of recurrence of carcinoma in the early postoperative period.

Comment

In empyema without fistula, decortication or extrapericostal air plombage usually is used; the former procedure is performed for a localized and the latter for an extensive empyema. However, the treatment of empyema with fistula is more varied because it often is difficult. The mortality in patients with a bronchial stump fistula after pneumonectomy is considerable. In the treatment of acute empyema resulting from bronchial fistula, we have performed an open-window thoracostomy as an emergency procedure. After daily irrigation with antibiotics, we then performed repeat closure of the bronchial stump and muscle plombage. The results, however, were sometimes not favorable. In elderly patients with bronchial carcinoma, the bronchial stump may be at risk of ischemia because of the dissection of surrounding tissues. Accordingly, in the case of a large bronchial stump with dehiscence due to ischemia, covering the fistula with a muscle flap alone will be inadequate because muscle lacks the ability of fat to promote angiogenesis [19]. For this reason, we used the omentum for closing bronchial stump fistulas in this series and obtained good results.

Several surgical techniques have been introduced for the treatment of chronic empyema with fistula. We have previously performed open-window thoracostomy followed by myoplasty in select patients, using methods reported previously [1–3, 5, 8]. For empyema with fistula, pleuropneumonectomy is a potentially curative operation, but it may be too invasive for patients at risk. Bronchial fistulas generally heal poorly owing to an inadequate blood supply and persistent infection [7]. The omentum has a rich blood supply and tends to adhere well to inflammatory tissue [7, 15]. In 21 empyemic patients, Hankins and colleagues [6] reported six recurrences and unsuccessful treatment in 4 patients; in 2 others, treatment was partially successful but myoplasty had to be repeated. Myoplasty is a safer procedure than pleuropneumonectomy or extended thoracoplasty, but myoplasty does not always provide satisfactory results in elderly or thin, malnourished patients.

The remarkable power of the omentum to aid tissue repair may result from its encouragement of cellular proliferation and fibrous tissue formation, as well as its adhesion to surrounding organs [10, 16, 18]. Furthermore, both the rich omental lymphatic system and the revascularization promoted by the omentum permit rapid reabsorption of inflammatory exudates, with little local infection [3, 15]. Miller and co-workers [20] reported good results in 2 patients who underwent closure of a postpneumonectomy empyema space with use of both extrathoracic muscle flaps and omental grafts. In this series, we also added plombage with chest wall muscles in a few patients in whom the thin omental tissue was not suffi-

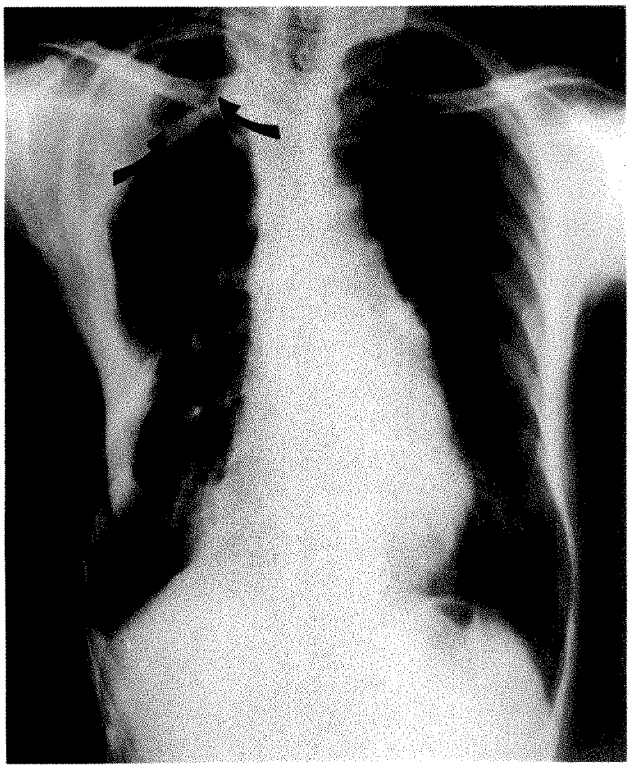

*Fig 4. A chest roentgenogram performed 6 months after operation in patient 4 shows the marked decrease in the right apical dead space (*arrows*).*

cient to cover the empyema surface. We do not believe that complete closure of an empyema space is always needed, however, provided that the residual space is kept clean by daily gauze dressings and provided that omental coverage of the fistula openings is sufficient. The residual space decreases considerably in such cases with time, even though it does not become completely obliterated. In 3 patients with chronic empyema, additional muscle plombage was not performed. All are now alive and well despite having a residual pleural space.

Based on their experience in chest wall reconstruction with omentum, Jurkiewicz and Arnold [11] stressed that the right gastroepiploic artery is usually lager than the left and that omental flaps accordingly should be based on the right gastroepiploic vessels. We believe that either artery may be used, although in all our patients the right gastroepiploic vessels were used for the blood supply of the flap. Use of the omentum should be avoided in patients who have had any previous operation on the gastrointestinal tract or who have any kind of active abdominal disease.

Regarding postoperative complications, subacute ileus with brief postoperative abdominal distention developed in only 1 patient. Although there is a theoretical risk of herniation of the abdominal organs, this complication did not occur in our series. When using an omental flap, one must be careful to avoid any kinking, compression, or rotation of the vascular pedicle [15]. Formation of larger hematomas in the omentum should also be avoided [12]. Infection may spread to the abdominal cavity because a passage is created surgically between the empyemic space and the abdomen, particularly in cases of pulmonary tuberculosis or aspergillosis. Therefore, to achieve sterilization of the empyema space, we recommend an open-window thoracostomy followed by daily gauze dressings for several months before its closure is attempted.

Two patients in our series had unsuccessful results. The cause of failure was considered to be that both patients were malnourished and had severe chronic infection of the airways and lung parenchyma. Thus, it appears that if the lung has foci of persistent infection with fistulas connecting to the empyema space, omental plombage may not be successful.

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Low-Dose Preoperative Aspirin Therapy, Postoperative Blood Loss, and Transfusion Requirements

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The effects of three low-dose regimens of preoperative aspirin therapy on postoperative blood loss, transfusion requirements, and length of hospital stay were recorded in a prospective cohort study of 202 patients undergoing elective coronary artery bypass grafting. One hundred one patients had been prescribed daily aspirin by the referring cardiologist (44 at 75 mg, 28 at 150 mg, and 29 at 300 mg); the remaining 101 patients who had not been prescribed aspirin acted as a control group. A median postoperative blood loss of 870 mL in the control group was increased by 280 mL in the 75-mg aspirin group ($p < 0.001$), by 490 mL in the 150-mg aspirin group ($p < 0.001$), and by 230 mL in the 300-mg aspirin group ($p = 0.03$). The median requirement for blood transfusion of 2 U red blood cell concentrates in the control group was increased by 2 U in the 75-mg aspirin group ($p < 0.001$), 2 U in the 150-mg aspirin group ($p < 0.001$), and 1 U in the 300-mg aspirin group ($p = 0.05$). Hemostatic "packs" (fresh frozen plasma, platelets, and cryoprecipitate) were required in 20 patients in the aspirin groups as compared with 5 in the control group ($p < 0.01$ by χ^2 test). The mean postoperative hospital stay was 8 days for all groups. Regular daily low-dose aspirin therapy produces significant increases in postoperative blood loss, resulting in a substantial increase in blood transfusion and hemostatic pack requirements, but does not prolong postoperative hospital stay.

(Ann Thorac Surg 1990;50:425–8)

The efficacy of aspirin in reducing the incidence of myocardial infarction in primary and secondary prevention trials [1] and in improving long-term patency of vein grafts after coronary artery bypass grafting when prescribed perioperatively [2] has resulted in increasing use of aspirin in patients awaiting coronary revascularization.

Most studies of aspirin as a prophylactic therapy for cardiovascular events have used daily doses of 300 to 1,500 mg. Evidence shows, however, that similar prophylactic efficacy can be achieved with doses as low as 50 mg/day without the increased incidence of side effects that occurs with doses greater than 300 mg/day [1].

For editorial comment, see page 345.

Studies of the effects of preoperative aspirin therapy on blood loss associated with cardiac operations have produced conflicting results; some groups of investigators have reported an increase [3–5], and others have reported no effect [2, 6, 7]. The largest of these studies, that of Goldman and associates [5], based on the results of a Veterans Administration Cooperative Study, reported that aspirin in daily doses between 325 and 975 mg did increase postoperative bleeding, but the effects of low-dose aspirin therapy on blood loss after cardiopulmonary bypass has not been addressed.

We compared the effects of differing low doses of preoperative, regular, daily aspirin therapy (75, 150, and 300 mg) with no preoperative aspirin intake on postoperative blood loss, blood product requirements, and postoperative hospital stay in 202 consecutive patients undergoing elective coronary artery bypass grafting.

Material and Methods

Patient Population

Two hundred two consecutive patients undergoing elective coronary artery bypass grafting were studied. Patients receiving warfarin or undergoing redo operations or combined coronary and valve operations were excluded from the study. In no case was aspirin administered for the purpose of the study.

All patients had chronic stable angina and were receiving regular antianginal medication consisting of β-blockers, nitrates, and calcium antagonists, singly or in combination. In addition, the 15 referring physicians had also prescribed daily aspirin in 101 of these patients awaiting coronary artery bypass grafting. Cardiologists prescribed preoperative aspirin in all or none of their patients depending on their particular clinical practice. The waiting time for operation was between 6 and 9 months. As far as could be ascertained by questioning and reviewing the case notes, the remaining 101 patients had not been taking aspirin or an aspirin-based medication regularly. Preoperative aspirin medication was continued until the morning of operation, and on the morning after operation

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all patients were started on 75 mg aspirin and 100 mg dipyridamole three times daily.

Six surgeons participated in the study using similar operating techniques (pulsatile cardiopulmonary bypass, bubble oxygenator, and moderate [28° to 30°C] hypothermia). In most patients, an internal mammary artery graft was used as part of revascularization.

Postoperative chest drainage was measured hourly until the time of drain removal. Chest drains were not removed until a minimum of 15 hours after operation and not until there had been 5 consecutive hours of drainage of less than 20 mL/h.

Prescription of hemostatic "packs" (consisting of 500 mL fresh frozen plasma, 5 U platelets, and 10 U cryoprecipitate) was made by the consultant surgeon or senior registrar, both of whom were unaware of the study in progress. The presence of an obvious surgical cause of bleeding at reexploration resulted in exclusion of 2 patients from further study, whereas bleeding attributable to coagulopathy did not.

The requirement for blood transfusion (350-mL units of red blood cell concentrates) was determined by the need to maintain the postoperative packed cell volume above 30%. The number of units of blood or blood products required by each patient was recorded by one author (A.S.) who was not responsible for their prescription.

Statistical Analysis

Results are expressed as mean and standard deviation (SD) except where data are clearly skewed, when the median and 95% confidence intervals (CI) are presented. The Kruskal-Wallis test was used to identify differences in postoperative blood loss and transfusion requirements among the groups, as these data were not normally distributed. A Mann-Whitney U test was used for follow-up when differences existed among the groups.

The χ^2 test with Yates' correction factor was used to analyze differences in the requirement for coagulation packs and the need for rethoracotomy in the control group as compared with the aspirin group as a whole. Multiple-regression analysis was used to determine which parameters (age, bypass times, number of grafts) significantly correlated with postoperative blood loss.

Results

Of the 202 patients studied, 101 had been prescribed daily aspirin (75 mg in 44, 150 mg in 28, and 300 mg in 29) while on the waiting list for operation (6 to 9 months). The remaining 101 patients had not been prescribed, nor did they admit to taking, regular aspirin therapy or other aspirin-based medication. Two of the patients not taking aspirin were excluded from further analysis because of an obvious surgical cause of bleeding at reexploration for excessive blood loss. The four groups were similar with respect to age, sex distribution, the number of bypass grafts performed (including use of internal mammary artery grafts), bypass times, and duration of chest drainage (Table 1).

Total blood loss in the four groups is shown in Figure 1.

Table 1. Summary of Patient Population, Operative Features, Hemostatic Pack Requirements, and Duration of Hospital Stay[a]

	Aspirin Dose (mg)			
Variable	0 (Control)	75	150	300
No. of patients	99	44	28	29
Age (y)	56 (9)	56 (9)	58 (6)	58 (8)
Males (%)	86 (87%)	33 (75%)	25 (89%)	24 (83%)
No. of grafts	3.0 (1.0)	3.1 (1.1)	3.3 (1.1)	3.1 (0.9)
IMA graft (%)	83 (84%)	34 (77%)	20 (72%)	26 (90%)
Bypass time (min)	84 (31)	84 (28)	95 (32)	88 (28)
Drainage (h)	25 (9)	28 (11)	30 (13)	24 (8)
Hemostatic packs	5 (5%)	12 (27%)	7 (25%)	1 (3%)
Hospital stay (d)	8.2 (2.5)	8.1 (2.4)	8.5 (2.6)	8.2 (2.1)

[a] Values are shown as mean and standard deviation.

IMA = internal mammary artery.

In the control group, the median postoperative blood loss was 870 mL (95% CI, 790 to 960 mL). The median postoperative blood loss increased in all groups receiving regular, daily aspirin therapy: an increase of 280 mL in patients receiving 75 mg aspirin daily (95% CI, 30 to 420 mL; $p = 0.02$), 490 mL in patients receiving 150 mg aspirin daily (95% CI, 230 to 770 mL; $p < 0.001$), and 230 mL in patients receiving 300 mg aspirin daily (95% CI, 20 to 380 mL; $p = 0.03$).

Multiple-regression analysis showed that preoperative aspirin ingestion significantly, but weakly, correlated with postoperative blood loss (regression coefficient, 519.1; SD, 155.4; t ratio, 3.34; $r^2 = 0.09$; $p < 0.001$). Postoperative blood loss did not correlate significantly with age, bypass time, or number of grafts received.

The median blood requirement in the control group was 2 U packed red blood cells (95% CI, 1.5 to 2.5 U). The median increase in postoperative blood transfusion was 2 U (95% CI, 1 to 2 U; $p < 0.001$) in patients receiving 75 mg aspirin daily, 2 U (95% CI, 1 to 3 U; $p < 0.001$) in patients receiving 150 mg aspirin daily, and 1 U (95% CI, 0 to 2 U; $p = 0.05$) in patients receiving 300 mg aspirin daily. Hemostatic products were required in 5% of the control group as compared with 20% of patients receiving aspirin ($p < 0.01$ by χ^2 test), owing almost entirely to increased requirements in the 75-mg and 150-mg aspirin groups but not the 300-mg group.

In total 13 patients required chest reopening for bleeding (7 patients in the aspirin group and 6 in the control group). At reexploration among all these patients, a surgical cause of bleeding was found in only 2 patients not receiving aspirin (in both cases, bleeding was from the distal internal mammary artery and both patients were excluded from further analysis). In the remaining 11 patients, 7 in the aspirin group and 4 in the control group (not significant), the bleeding was attributed to coagulopathy as no specific site of surgical bleeding could be identified.

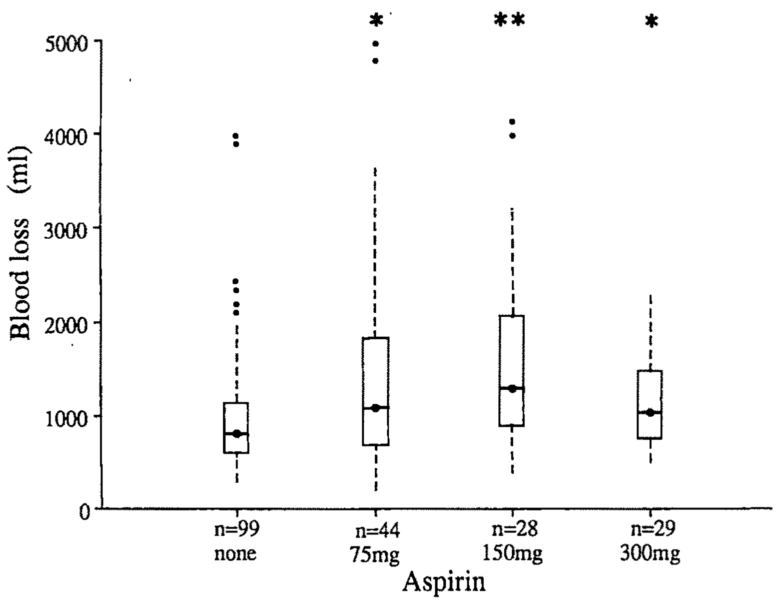

Fig 1. Box-plot and whisker diagram shows total blood loss in the four groups of patients ($p < 0.05$; ** = $p < 0.01$ as compared with control group). Center box shows median and interquartile range with whiskers indicating range of data, except for outliers, which are marked individually* (solid black dot).

The mean postoperative hospital stay was 8 days for all patient groups (see Table 1).

Comment

This study is one of the largest yet reported to examine the effects of regular daily preoperative aspirin therapy on postoperative blood loss. Although the study was not randomized, a selection bias is unlikely to have arisen as the decision to prescribe aspirin and the choice of dose were made by 15 cardiologists unaware of the proposed study, as were the operating surgeons during the study period. Individual cardiologists either prescribed aspirin for all or none of their patients depending on their particular clinical practice.

The similarity of the groups with respect to age, sex distribution, number of grafts received (including internal mammary artery grafts), and bypass times appears to confirm that no selection bias existed. Because thromboxane B_2 levels were not measured in serum, the possibility that control patients may have taken over-the-counter preparations with aspirinlike activity cannot be excluded on history alone. Such preparations, however, would have been likely to have predisposed patients in the control group to increased bleeding and would therefore have minimized any differences between the groups.

All aspirin groups had increased postoperative blood loss and transfusion requirements, although this was least marked in the 300-mg group. In platelets, aspirin irreversibly inhibits cyclooxygenase, preventing formation of thromboxane A_2, a potent stimulator of platelet aggregation [1]. Conversely, inhibition of cyclooxygenase in vascular endothelium prevents formation of prostacyclin, which inhibits platelet aggregation and induces vasodilatation [1]. Aspirin therefore has the potential, at least theoretically, to be both antithrombotic and thrombogenic. This potential has been used to explain the "aspirin paradox," in which increasing single doses of aspirin up to 1 g prolong bleeding time; at doses of more than 1 g, a return toward normal occurs [8, 9]. The ideal antithrombotic dose of aspirin therefore would be that which blocks cyclooxygenase in platelets but not in the vascular wall; this is the rationale for current low-dose aspirin therapy. The possibility that the aspirin paradox may exist when aspirin is administered in daily doses between 75 and 300 mg has not been reported previously. It is conceivable that daily low-dose aspirin therapy may have a cumulative effect, leading to blood levels similar to those obtained with single larger doses, known to produce the aspirin paradox [8, 9]. Confirmation of this possibility requires pharmacological investigation and may help define optimal low-dose aspirin therapy. Alternatively, different preoperative doses of aspirin therapy may variably influence platelet damage induced by extracorporeal perfusion but, again, confirmation of this would require detailed investigation.

In our study, use of preoperative aspirin, but not age, bypass time, or number of grafts received, was an independent predictor of postoperative blood loss as determined by multiple-regression analysis. The correlation coefficient was low, however, implying that preoperative use of aspirin may be a good predictor of increased blood loss in a group of patients but not in individual patients. A recent publication by Ferraris and Gildengorin [10] could not confirm preoperative aspirin therapy as a predictor of postoperative bleeding; however, of 159 patients studied by these investigators, only 15 had received preoperative aspirin therapy. Ferraris and Gildengorin [10] did identify blood cell volume, derived from preoperative hematocrit and blood volume (derived from a nomogram based on patient weight, height, and sex), as an independent predictor of postoperative blood loss. We did not address this question specifically in our study, but as our patients formed a homogenous group who had not been hospitalized for the 6 months preceding operation, we would not expect significant differences in blood cell volume.

The increased transfusion requirements in the aspirin groups were greater than would be expected from the observed increases in postoperative chest drainage. However, prophylactic aspirin therapy probably also predisposes to increased intraoperative blood loss, which is difficult to quantitate and which was not included in the postoperative losses in this study.

Our results suggest that preoperative low-dose aspirin therapy approximately doubles blood transfusion requirements and substantially increases the need for hemostatic products after coronary artery bypass grafting. Because coronary artery bypass grafting is one of the most commonly performed major operations in the United Kingdom, the implications for reducing the risk of transfusion-transmittable diseases in individual patients as well as demands on transfusion services are substantial.

Aspirin therapy significantly alters platelet function within a few hours of administration and prolongs bleeding times for at least the subsequent 7 days [11]. To reverse this effect therefore would require that aspirin therapy be stopped at least 1 week before operation. It is unlikely that such a policy would predispose patients to a significant increase in the risk of a fatal or nonfatal coronary event; the Aspirin Myocardial Infarction Study Research Group trial of prophylactic aspirin therapy in patients with documented ischemic heart disease reported only a small decrease in coronary events (from 14.8% to 14.1%) over a 3-year period [12]. It is also unlikely that such a policy would jeopardize the long-term patency of aortocoronary bypass grafts. Platelet numbers and function decrease with cardiopulmonary bypass [13]; because aspirin affects platelet function within 2 hours of administration [11], aspirin therapy started postoperatively once bleeding has ceased should achieve platelet inhibition rapidly. Lorenz and colleagues [2] showed such a policy to be effective by demonstrating that starting aspirin therapy (100 mg) within the 24-hour period after coronary artery bypass grafting improves angiographically confirmed long-term patency of saphenous vein grafts [2].

Although it is difficult to make definitive recommendations based on the results of our study, we suggest that discontinuing aspirin medication for 1 week before a coronary operation would result in a significant reduction in blood product requirements and the attendant risks of transfusion without any increase in cardiovascular morbidity. Furthermore, if aspirin therapy subsequently is restarted in the early postoperative period when blood loss has reached minimal levels (usually within 6 hours after operation), the long-term patency of aortocoronary grafts probably will not be jeopardized.

We thank Margaret Whiteside for typing the manuscript.

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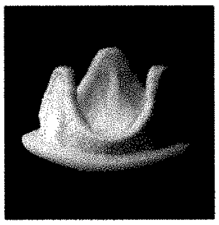

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The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile**. The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions: 1.** When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. 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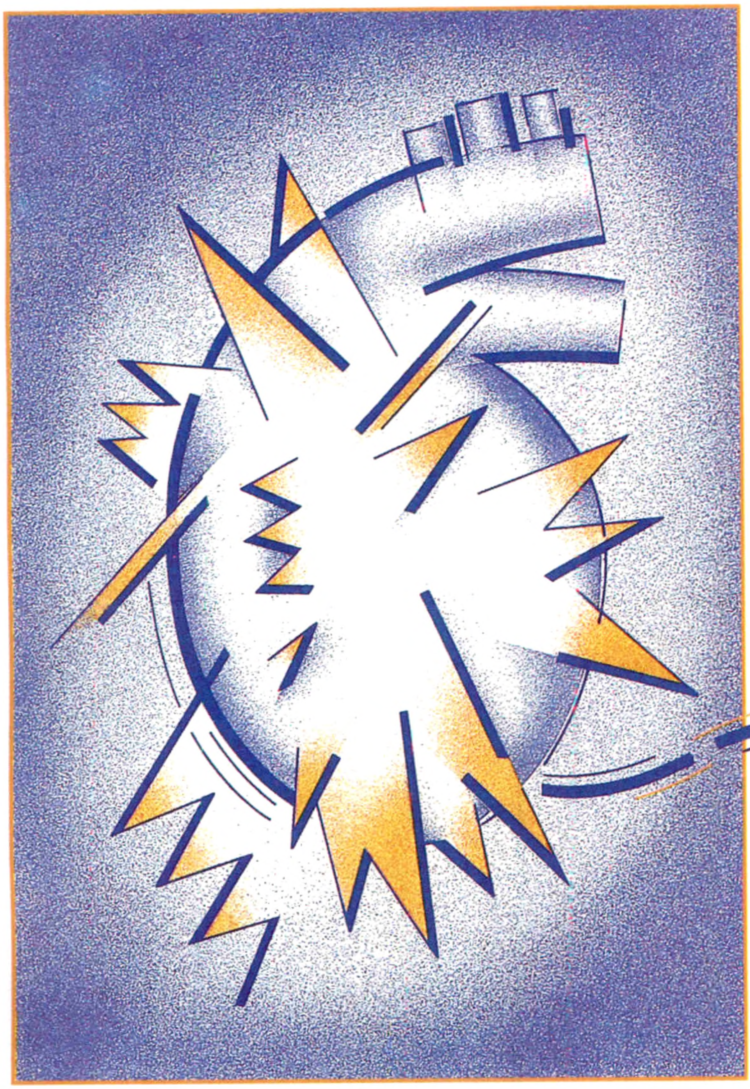

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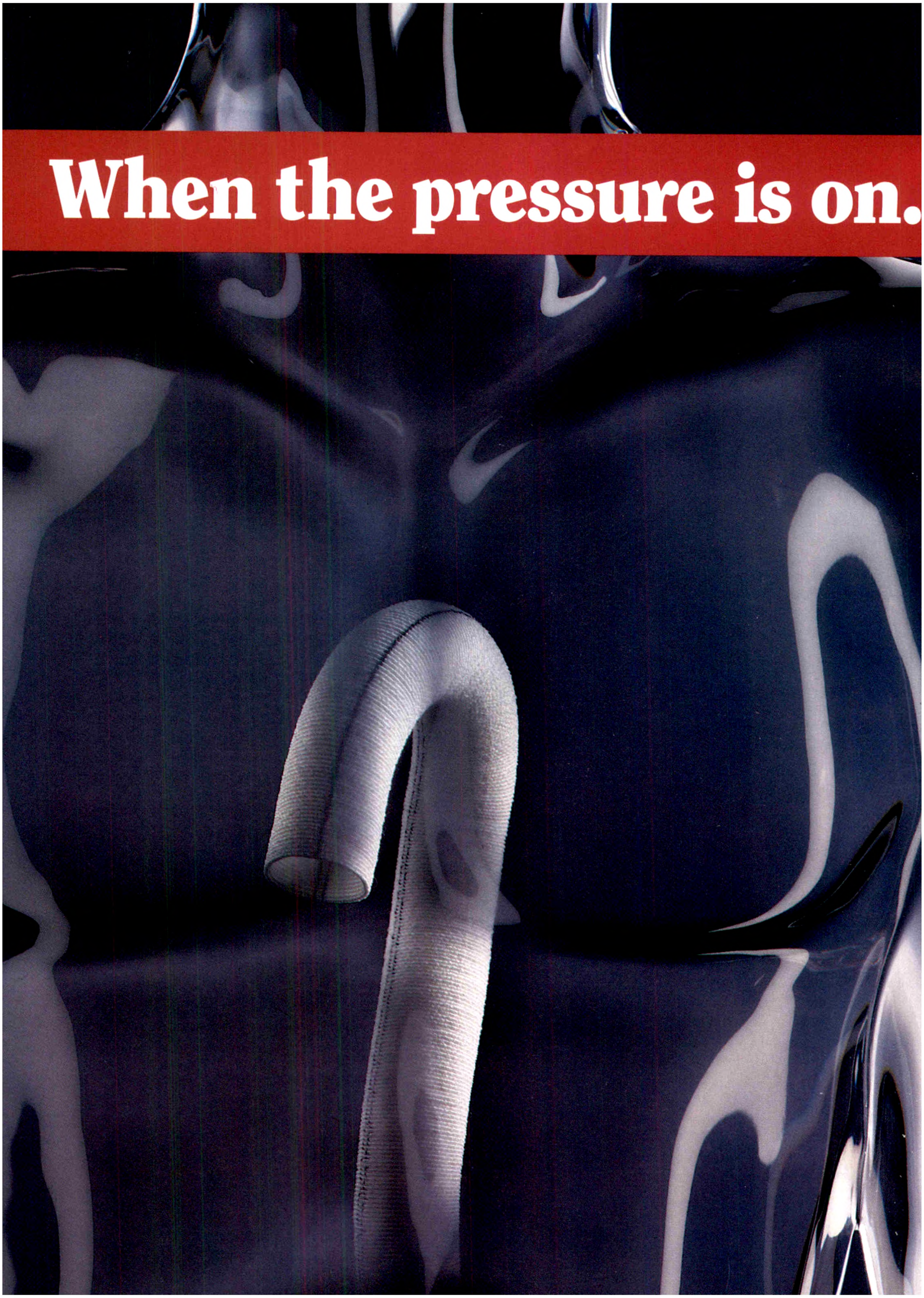
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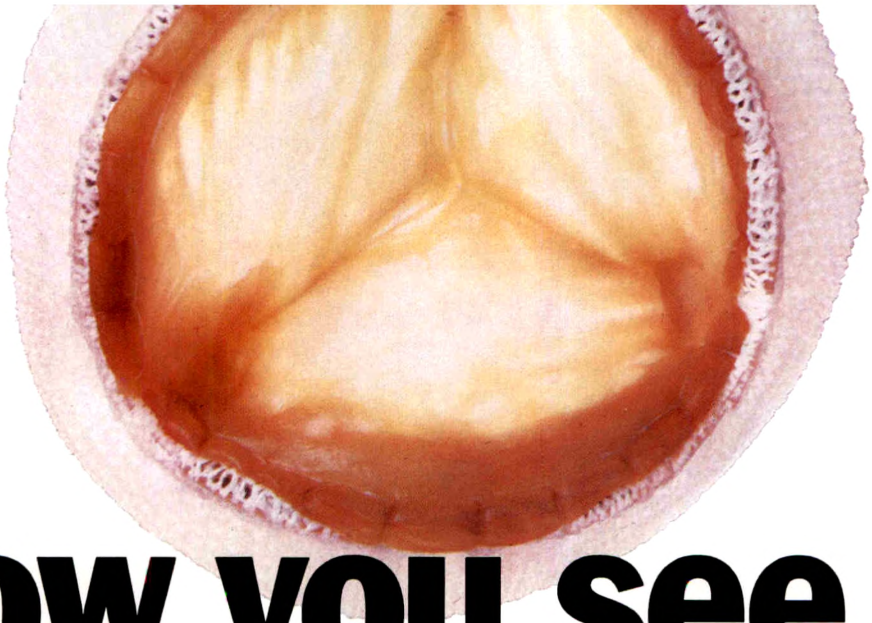

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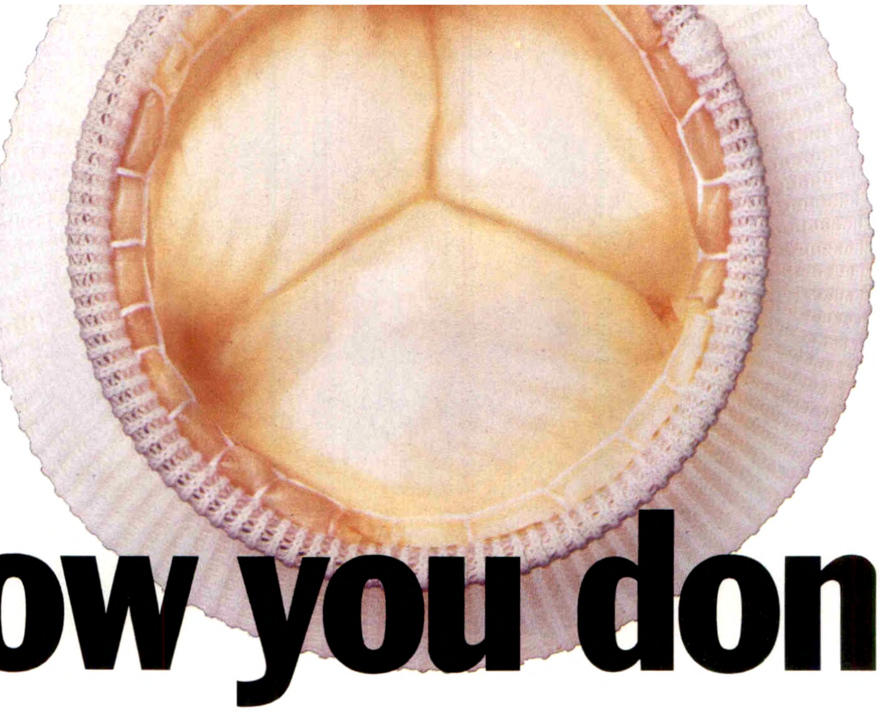

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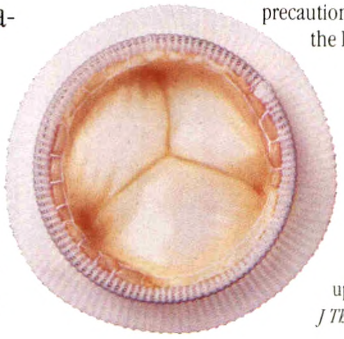

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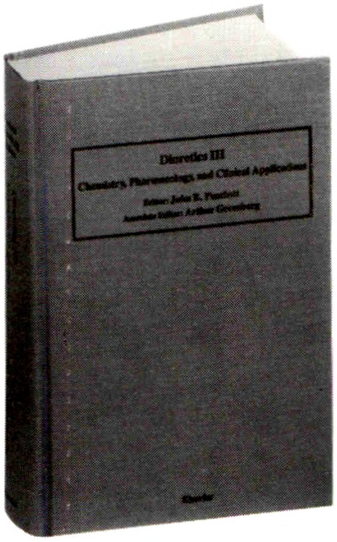

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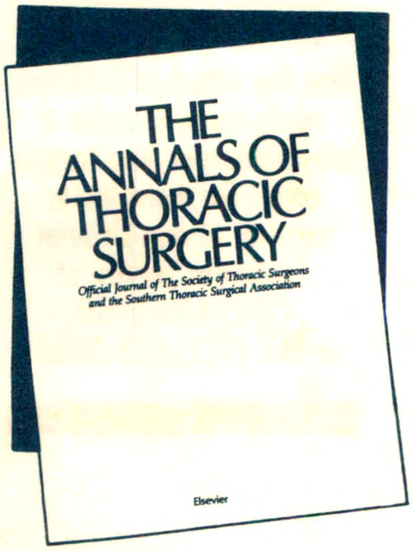
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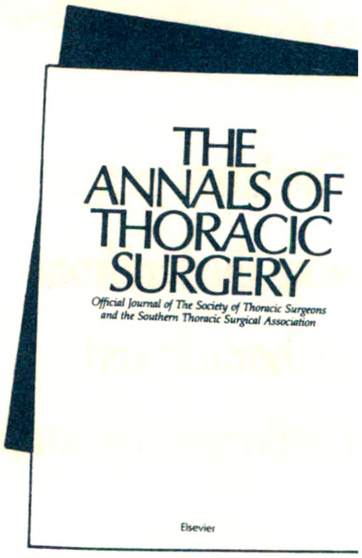
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Eight Years' Experience With the Medtronic-Hall Valve Prosthesis

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During the period January 1981 to September 1986, 444 Medtronic-Hall heart valve prostheses were implanted in 351 patients (mean age, 45 ± 10 years) mainly for rheumatic valve disease (63.2%). Most of the patients were in New York Heart Association functional class III. Concomitant surgical procedures, mainly conservative tricuspid or mitral procedures or coronary artery bypass grafting, were performed in 101 patients (28.7%). Single-valve replacement was performed in 262 patients (74.6%) (aortic in 117 patients, mitral in 143, and tricuspid in 2), double-valve replacement in 85 (24.2%) (mitral and aortic in 83 and mitral and tricuspid in 2), and triple-valve replacement in 4 (1.1%). Hospital mortality was 6.2%. Follow-up was 97.7% complete. The overall actuarial 8-year survival rate was 77.2%. The linearized incidence of valve-related complications was as follows: thromboembolism, 1.5%/patient-year; reoperation, 1.5%/patient-year; endocarditis, 1.25%/patient-year; hemolysis, 0.52%/patient-year; anticoagulant-related hemorrhage, 0.39%/patient-year; and noninfection-related paraprosthetic leak, 0.33%/patient-year. There were no instances of structural failure. We conclude that after 8 years of follow-up, the Medtronic-Hall valve prosthesis has an excellent clinical performance and a low range of valve-related complications.

(Ann Thorac Surg 1990;50:429–36)

Since the introduction of the disc valve prosthesis in 1969, various series have demonstrated the good results obtained with these devices [1–6]. In spite of this improvement, we are still looking for the ideal prosthesis. In January 1981, we began to implant the low-profile, pivoting-disc (pyrolytic carbon) Medtronic-Hall mechanical valve prosthesis. What interested us in this particular prosthesis were mechanical features suggesting the possibility of better hemodynamic performance: the wide opening angle (75 degrees) and the upward gliding movement of the disc [7]. The wide disc movement would facilitate flow through the prosthesis, thus allowing reduction in the rate of thromboembolism. The central orifice ensures a secure attachment, thus preventing disc migration.

For editorial comment, see page 346.

Our usual practice is to implant porcine bioprostheses in older patients (older than 70 years), in young patients who request it, and in patients for whom anticoagulation is contraindicated. In the remaining patients, we use mechanical prostheses: Medtronic-Hall, Björk-Shiley, and St. Jude Medical. These prostheses were considered to have potentially better characteristics than others available at the time, but the preference of the surgeon led to the final choice.

The purpose of this study was to analyze our clinical experience with the Medtronic-Hall valve prosthesis in patients followed up for 27 months to 8 years postoperatively.

Material and Methods

During the period January 1981 to September 1986, 444 Medtronic-Hall valve prostheses were implanted in 351 patients operated on in our department. There were 283 female and 68 male patients with a mean age of 45 ± 10 years (range, 9 to 64 years).

Most of the patients were in New York Heart Association functional class III preoperatively. Atrial flutter or fibrillation was present in 50.7% (178 patients). One hundred one patients had previously undergone 112 heart operations. In 21 of these patients, the operation had been carried out on an emergency basis. The cause was rheumatic in most instances, followed in order of frequency by degenerative conditions, calcification of bicuspid aortic valves, and prosthetic valve dysfunction. The main clinical data are shown in Table 1.

Follow-up was 97.7% complete and totaled 1,510.3 patient-years. The cutoff date was December 1988, so that the minimum follow-up was 27 months and the maximum, 8 years.

Data were collected in most instances by direct examination of the patients. When that was not possible, questionnaires and telephone contact, either with the patients themselves or with their cardiologists, were used.

The statistical treatment was based on Statgraphics

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Table 1. Preoperative Clinical Data

Variable	No. of Patients[a]
Age (y)[b]	45 ± 10 (9–64)
Sex	
Female	283 (80%)
Male	68 (20%)
Atrial fibrillation	178 (50.7%)
Previous valve procedure	101 (112 operations)
Emergency operation	21
Cause	
Rheumatic	222
Degenerative	51
Bicuspid aortic valve	27
Bacterial endocarditis	19
Prosthetic dysfunction	
Biological	14
Mechanical	8
Ischemic	3
Other	7
NYHA functional class	
I	15 (4%)
II	60 (17%)
III	221 (63%)
IV	55 (16%)

[a] Data are shown as number of patients unless otherwise stated. [b] Datum is shown as the mean ± the standard deviation with the range in parentheses.

NYHA = New York Heart Association.

(Statistical Graphics System) by Statistical Graphics Corporation, which performs actuarial analysis of the valve-related events. A p value of less than 0.05 was considered significant.

Surgical Technique

All surgical procedures were performed by the same surgical team with conventional cardiopulmonary bypass and a bubble oxygenator. In some instances when prolonged cardiopulmonary bypass was anticipated, membrane oxygenators were employed. Operations were performed under moderate hypothermia (28°C). For myocardial protection, continuous topical hypothermia was used, and crystalloid cardioplegic solution was administered in repeated injections to the aortic root or through both coronary ostia when the nature of the operation necessitated the opening of the aorta. Myocardial temperature was monitored continuously to ensure adequate myocardial protection (10° to 15°C). The average time of aortic clamping was 54 ± 20 minutes.

The valves were fixed with interrupted mattress sutures (2-0 Ticron) reinforced with Teflon pledgets in the annulus. The opening of the prosthetic disc was generally oriented to the interventricular septum (anteriorly) in mitral procedures and to the commissure of the noncoronary and right coronary cusps in aortic procedures. In every operation, the basic approach was to ensure freedom of disc movement.

Surgical Procedures

In 117 patients, only the aortic valve was replaced. In 143 patients, isolated mitral valve replacement was done. In 83 patients, both the mitral valve and the aortic valve were replaced. On four occasions, the aortic, mitral, and tricuspid valves were replaced. Two patients had isolated replacement of the tricuspid valve because of Ebstein's disease (1 of these patients represented a complex case with pulmonary atresia and a right ventricle to pulmonary artery valved conduit). Two patients underwent mitral and tricuspid valve replacement. The sizes of the prostheses used are shown in Table 2.

Associated procedures were performed in 101 patients: mitral commissurotomy, 14 patients; mitral annuloplasty (Carpentier's ring), 3; tricuspid annuloplasty (Carpentier's ring), 64; tricuspid annuloplasty (De Vega), 5; coronary artery bypass grafting, 14; and aortic annulus enlargement (Manouguian), 1 patient.

Anticoagulant Regimen

All patients began anticoagulant treatment with low doses of heparin calcium (2,500 U every 8 hours), administered subcutaneously 24 hours postoperatively once drainage had ceased. Forty-eight hours after operation and simultaneously with removal of the chest tubes, anticoagulation with acenocoumarol (Sintrom) was initiated in daily doses of 3 mg without discontinuation of heparin. On the third postoperative day, the administration of heparin was interrupted if prothrombin activity was adequate (international nationalized ratio = 3 to 4.5 [1.5 to two times control]) [8]. Thereafter Coumadin (crystalline warfarin sodium) alone was used. Every pregnant patient was under the care of her own physician.

Definitions

The definitions used were those of The Society of Thoracic Surgeons [9] and The American Association for Thoracic Surgery.

Hospital Mortality: death occurring within the first 30 days after operation or within any interval if the patient is not discharged from the hospital.

Thromboembolism: any valve thrombosis or embolus except when associated with infection. Included in

Table 2. Prosthetic Valve Sizes

	Size (mm)					
Valve Replaced	21	23	25	27	29	31
Aortic	30	61	54	46	13	0
Mitral	0	0	8	84	119	21
Tricuspid	0	0	0	2	3	3

this category is any transient or permanent episode, global or focal, arising from a neurological deficiency. Excluded are patients who do not awake after operation or who awake with a stroke or myocardial infarction. Only a myocardial infarction that occurs in a patient with known normal coronary arteries can be defined as a thromboembolic event.

Anticoagulant-related hemorrhage: any episode of external or internal bleeding that leads to death or hospitalization or that necessitates blood transfusion in patients receiving permanent anticoagulant treatment.

Prosthetic valve endocarditis: any infection that affects the heart or a prosthesis and is confirmed by clinical criteria (blood cultures or anatomical and pathological findings).

Hemolysis: classified into three degrees according to Volkmer and associates [10]: mild, moderate, and severe. Patients with paravalvar leaks were excluded.

Results

Hospital Mortality

A total of 22 patients (6.2%) died in the hospital. The highest mortality rate was noted in the group having tricuspid valve replacement and the lowest, in the group who had isolated aortic valve replacement (Table 3). Also conspicuous was the low mortality rate in the group who underwent double-valve replacement of aortic and mitral valves in comparison with the group who had isolated mitral valve replacement. The only significant difference was the mortality rate for the isolated aortic valve replacement group versus that of the isolated mitral valve replacement group ($p < 0.0002$).

In most instances, death was due to low cardiac output syndrome or right ventricular failure (Table 4). On two occasions, rupture of the atrioventricular sulcus supervened as a result of excessive resection of calcified mitral valves. In the eight noncardiac deaths, sepsis was the most frequent cause (4 patients, 2 of whom were operated on for paraprosthetic leaks).

A logistic univariate study was used to determine which variables were related to intraoperative or postoperative death. Atrial fibrillation ($p < 0.05$), age greater than 40 years ($p < 0.0025$), a prolonged aortic cross-clamp time (longer than 60 minutes) ($p < 0.0001$), New York Heart Association functional class III or IV ($p < 0.001$), and moderate (40 to 60 mm Hg) to severe (greater than 60 mm Hg) pulmonary artery pressure ($p < 0.0002$) significantly influenced mortality.

Table 3. Hospital Mortality

Valve or Valves Replaced	%
Aortic	1.70 (2/117)
Mitral	8.39 (12/143)
Mitral + aortic	6.02 (5/83)
Mitral + tricuspid	50 (1/2)
Aortic + mitral + tricuspid	25 (1/4)
Isolated tricuspid (Ebstein)	50 (1/2)
Total hospital mortality	6.26 (22/351)

Table 4. Causes of Hospital Death

Cause	No. of Patients
Cardiac related	
Low-output syndrome + arrhythmias	4
Right ventricular failure	4
Left ventricular failure	2
Rupture of left ventricle	2
Sudden death	1
Neurological sequelae	1
Noncardiac related	
Sepsis	4
Postoperative hemorrhage	1
Perioperative stroke	2
Anaphylactic shock	1

Late Mortality

There were 43 late deaths (13.0%), 27 (8.2%) of which were cardiac related. Chronic heart failure was the most frequent cause, and sudden death occurred five times. In 1 patient, a low cardiac output syndrome developed suddenly, the cause of which could not be identified. In 1 patient with endomyocardial fibrosis [11], progression of the disease was the cause of death.

The overall survival rate according to the actuarial method was 77.2% ± 2.8% after 8 years (Fig 1). The highest rate belonged to the group having isolated aortic valve replacement and the worst rate, to the group having mitral and aortic valve replacement (Fig 2). There were no significant differences.

Patients Lost to Follow-up

We lost track of 8 patients. Five were lost after discharge from the hospital. The other 3 were seen once for clinical checkups at 1 month, 12 months, and 17 months postoperatively. At that time, their condition was good.

Thromboembolism

There were a total of 23 episodes of thromboembolism in 21 patients (1.5%/patient-year). In the group of patients having isolated aortic valve replacement, the incidence was 0.72%/patient-year. In the group with isolated replacement of the mitral valve, it was 1.5%/patient-year and in patients having both mitral and aortic valve replacement, 2.86%/patient-year. There was a significant difference between the group having aortic valve replacement versus the group having double-valve replacement ($p < 0.02$).

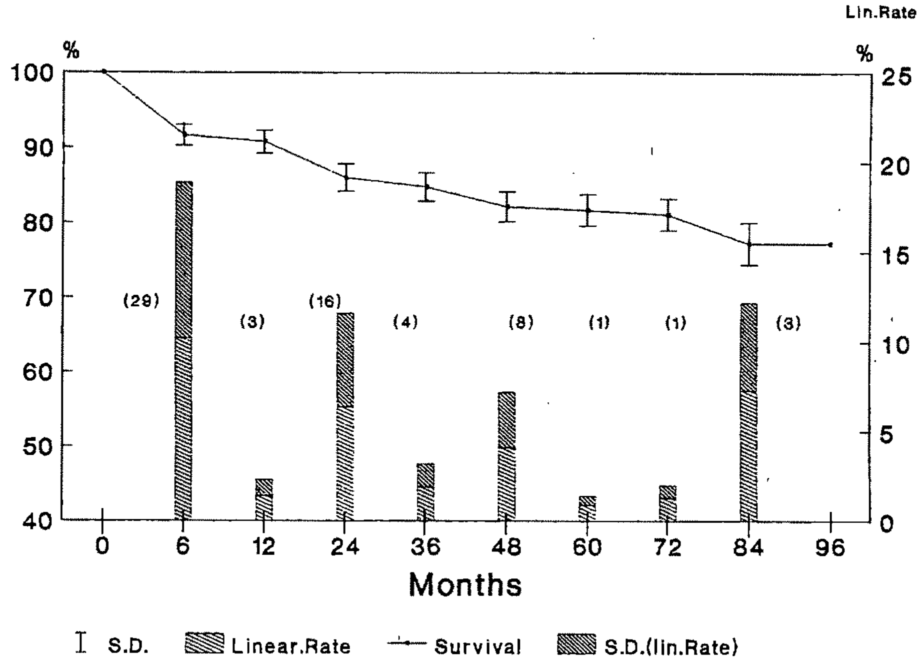

Fig 1. Overall actuarial survival curve, including operative mortality, and linearized rates. The number of events in each period is shown in parentheses. (S.D. = standard deviation.)

The actuarial method was employed to study patients in the thromboembolism-free group (Figs 3, 4), which comprised 90.9% ± 2% of patients at 8 years. The annual linearized rate showed that the chance of sustaining a thromboembolic event was greater in the first 2 years. Subsequently, there were two other periods of heightened risk: one in the fifth postoperative year and the other in the seventh postoperative year, although there was not a significant difference. The highest incidence of thromboembolism occurred in the patients having both aortic and mitral valve replacement.

The only prosthetic valve thrombosis occurred in a patient during the eighth month of pregnancy. She was admitted on an emergency basis with acute pulmonary edema, inaudible prosthetic valve sounds, and immobilization of the prosthetic disc, which was confirmed by roentgenography. A cesarean section was performed, followed by a hysterectomy and thrombectomy of the prosthesis. Both mother and child had a satisfactory course thereafter [12].

Anticoagulant-Related Hemorrhage

There were six instances of major hemorrhage related to anticoagulant treatment. In 3 patients, the hemorrhage

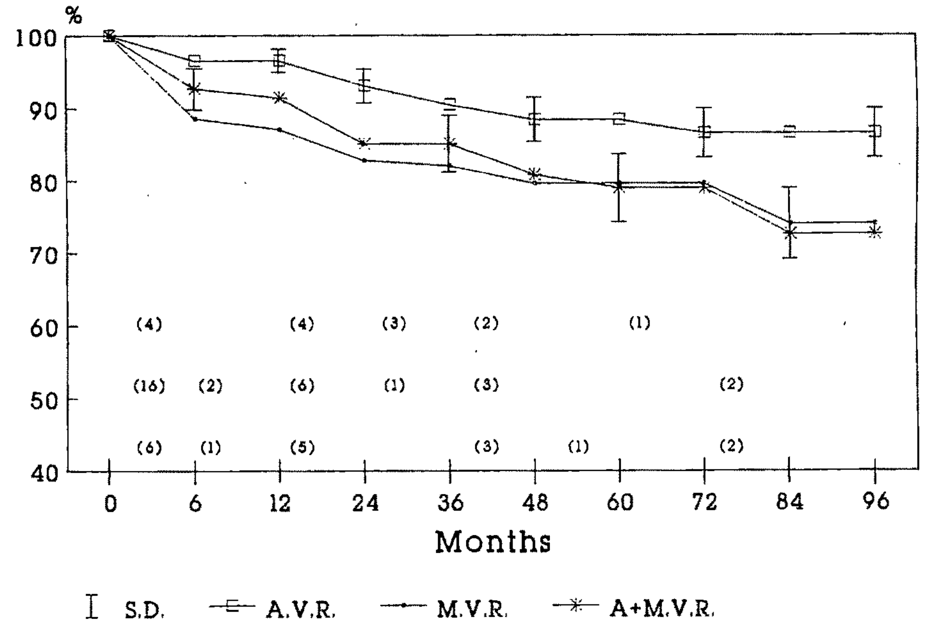

Fig 2. Actuarial survival curves for these groups. The number of events in each period is shown in parentheses. (A.V.R. = aortic valve replacement; A + M.V.R. = aortic + mitral valve replacement; M.V.R. = mitral valve replacement; S.D. = standard deviation.)

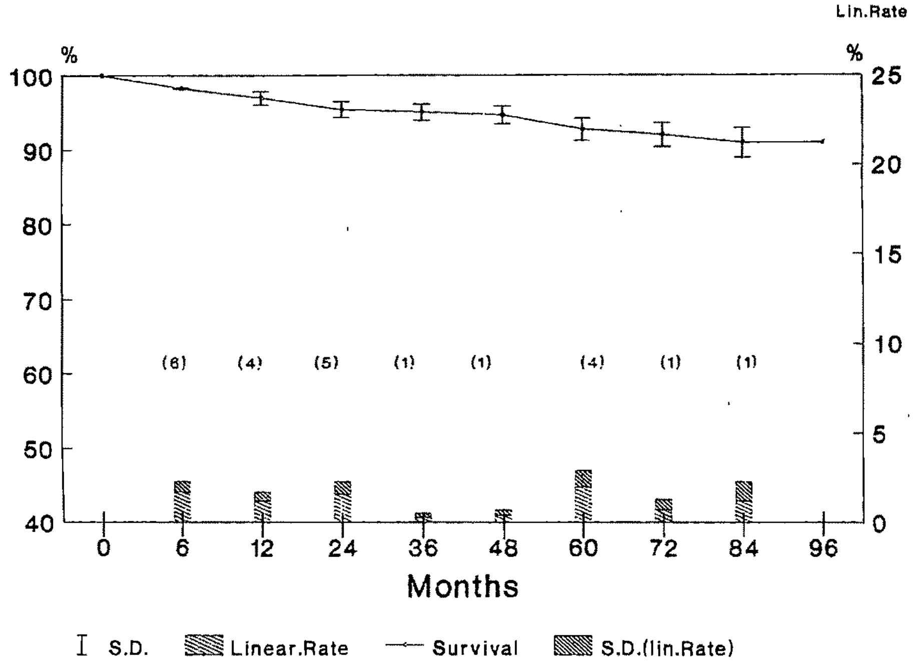

Fig 3. Actuarial curve of freedom from thromboembolic episodes and linearized rates. The number of events in each period is shown in parentheses. (S.D. = standard deviation.)

was fatal (two cerebral hemorrhages and one gastrointestinal hemorrhage). Another patient had to undergo gastric resection. The linearized rate was 0.39%/patient-year.

Endocarditis

There were 19 instances of endocarditis, a linearized incidence of 1.25%/patient-year. Figure 5 shows the actuarial curve of patients free from endocarditis, 93.11% ± 1.7% at 8 years postoperatively. The annual linearized rate indicated that the risk remained the same throughout follow-up.

The organisms involved were *Staphylococcus epidermidis* (8 patients), *Staphylococcus aureus* (3), *Candida albicans* (1 patient), and *Streptococcus viridans* (1); blood cultures were negative in 6 patients. Thirteen patients underwent reoperation (re-replacement of the prosthesis). Three of them had to undergo another reoperation. Mortality due to endocarditis was 36.8% (7/19 patients).

Hemolysis

Hemolysis was found in 8 patients. In 2, the cause was not mechanical. In the other patients, the cause was prosthetic, either intrinsic or due to dehiscence that had

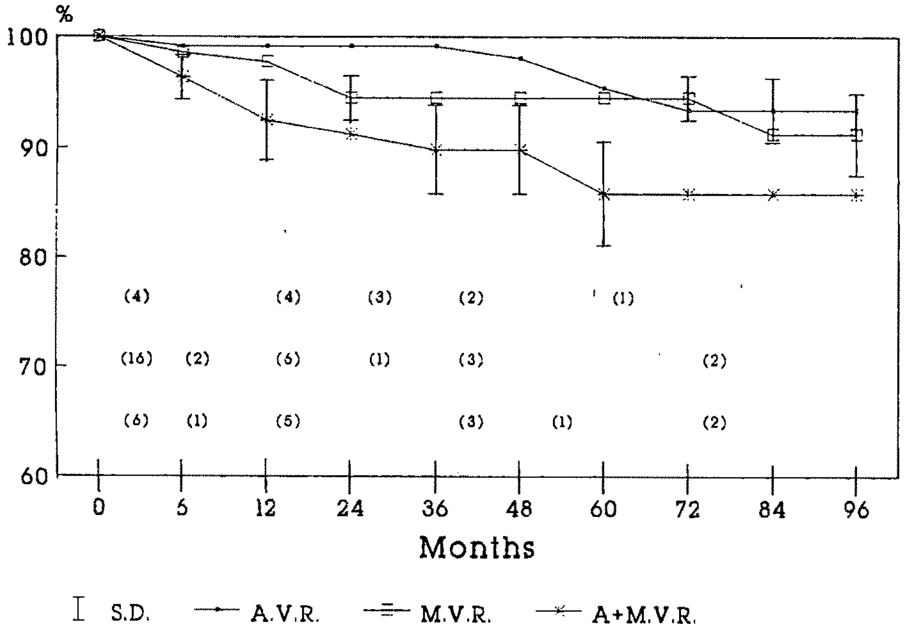

Fig 4. Actuarial curves of freedom from thromboembolic episodes for three groups. (A.V.R. = aortic valve replacement; A + M.V.R. = aortic + mitral valve replacement; M.V.R. = mitral valve replacement; S.D. = standard deviation.)

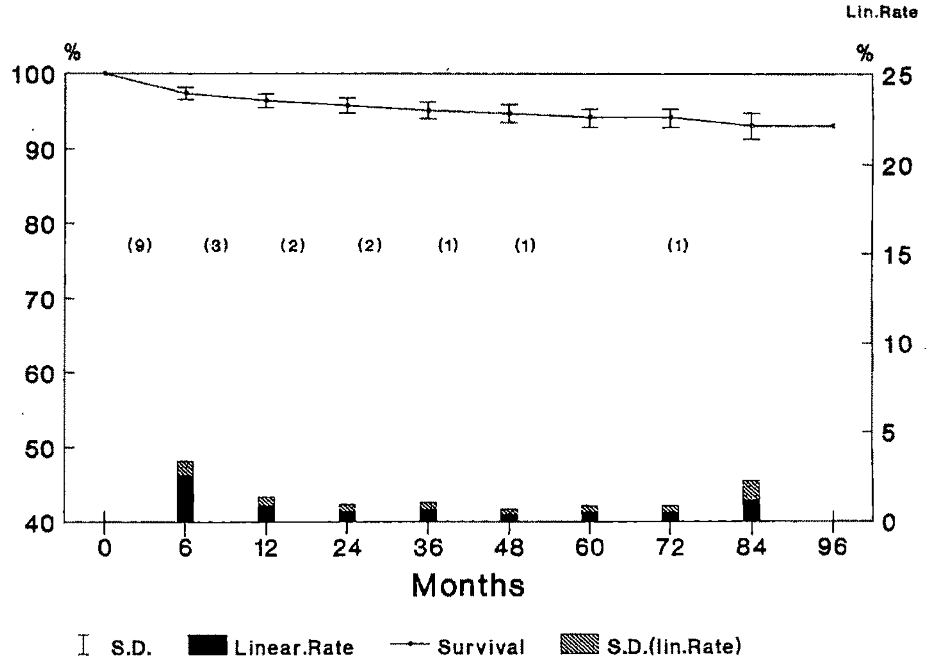

Fig 5. Actuarial curve of freedom from endocarditis and linearized rates. The number of events in each period is shown in parentheses. (S.D. = *standard deviation.)*

escaped clinical detection. The linearized incidence was 0.52%/patient-year.

Dehiscence

Five patients were found to have periprosthetic dehiscence due to noninfectious causes, although 1 of the patients had had a fever but negative blood cultures in the initial postoperative period. In another, a continuous suture was used instead of the interrupted suture technique usually employed by our team. We subsequently reoperated on this patient. Two patients had dehiscence several months after discharge from the hospital, the dehiscences probably due to the poor quality of the annular tissue after three previous valve replacements. The remaining patient will shortly undergo reoperation. The linearized incidence was 0.33%/patient-year.

Pregnancy

Seven patients became pregnant and delivered without teratogenic or hemorrhagic complication. One patient required a cesarean section. One patient had three normal pregnancies and deliveries after operation. One patient had thrombosis of the prosthesis because of poor management of anticoagulant treatment during pregnancy, as already described. A postpartum sepsis developed in another patient and necessitated replacement of the mitral and aortic prostheses. Her subsequent progress was satisfactory.

Reoperations

Twenty-three reoperations have been necessary. No reoperation was performed because of intrinsic failure of the prosthesis. The most frequent reason for reoperation has been endocarditis (17 reoperations). Noninfection-related prosthetic dehiscence led to four reoperations. One reoperation was due to thrombosis of the prosthesis and another, repeated thromboembolic episodes. The 23 reoperations represent a linearized incidence of 1.5%/patient-year.

Comment

Replacement of heart valves is, at present, a very well established treatment, though we are still far from finding the ideal valve prosthesis. Hence, different types of valve prostheses appear periodically on the market, and the possibility of an improved performance prompts surgeons to try them in their patients.

In our department, we began to use the Medtronic-Hall pyrolytic carbon pivoting-disc prosthesis because we were intrigued by the new design of its mechanism, which we thought might produce better results than we had obtained to date [7]. The large angle of aperture and the ample area of the minor orifice led us to assume that this prosthesis would give a better hemodynamic performance. We have had occasion to recatheterize some of our patients and were able to verify the fine hemodynamic characteristics of the prosthesis, findings in agreement with those in other reports [13–15]. We have obtained good results with good exercise performance in those patients in whom a small valve was used (21 mm for the aortic and 25 mm for the mitral position).

The fact that the prosthesis has an almost central flow caused us to believe that the incidence of thromboembolism would be reduced. In this series, that incidence has indeed been low and comparable with the best results reported [16–21]. A higher thromboembolic incidence with this prosthesis has been described [2], but it was in a third-world population in whom an adequate anticoagulant regimen was not carried out.

Thrombosis of the prosthesis occurred only once. It happened during the eighth month of pregnancy in a patient who had not received proper anticoagulant treatment. After thrombectomy, the patient progressed quite satisfactorily and returned to functional class I and a conventional anticoagulant regimen. We have had several experiences with other types of mechanical prostheses in which thrombectomy has been effective, as reflected in the literature [22, 23].

The threat of hemorrhage has always cast a shadow over valve replacement with mechanical prostheses. This is an area where bioprostheses have a clear advantage. In our practice, we use bioprostheses in older patients and in patients who live in rural areas where adequate supervision of anticoagulant treatment is not available.

On several occasions we have had young female patients who wanted to have children; in these patients we used porcine biological prostheses. We also have used the bioprosthesis in patients who specifically requested it. We normally use Björk-Shiley, St. Jude Medical, and Medtronic-Hall mechanical prostheses in treating the rest of our patients.

We have seen no instance of intrinsic dysfunction of the prosthesis. In most cases, reoperation has been related to the presence of endocarditis. In 1 patient, prosthetic dehiscence was due to the use of continuous suture on a calcified annulus.

Malfunction of the prosthetic disc has occurred intraoperatively on four occasions. Three times this was due to unraveled sutures that produced disc impingement. In the remaining instance, the cause of disc blockage was an excessively long chorda tendinea. All four malfunctions were detected because an elevated left atrial pressure was noted while the patient was on cardiopulmonary bypass. The situation was corrected with no further problems.

In one instance, it was discovered in the intensive care unit that the prosthetic disc opened once every two heart beats. This was verified by monitoring the electrocardiogram and arterial pressure. The patient underwent reoperation at which it was confirmed that the valve was too large and the wall of the left ventricle hindered disc movement. Similar cases of dysfunction with various types of prosthetic disc valves have been described in the literature. This complication has sometimes caused death [24]. We think it is of paramount importance to check the pressure in the left atrium to detect this complication and rectify the situation while the chest is still open.

The only patient who died suddenly in the hospital underwent postmortem examination. It was confirmed that death was not due to any prosthesis-related problem.

During follow-up, 7 patients became pregnant. We found that anticoagulation was not properly controlled during this period. One of these patients sustained the only prosthetic thrombotic event in the series. In another patient, endocarditis made replacement of the aortic and mitral valve prostheses necessary.

No teratogenesis resulting from the use of anticoagulants was recorded in this series. Hemodynamic performance during pregnancy and delivery was good in all patients. Although complications arose in only 2 patients in our series, the experiences of other authors [25–27] demonstrate that pregnancy can be considered a genuine complication in patients with mechanical prostheses and receiving anticoagulant treatment for an indefinite period.

We found that on admission to the hospital, pregnant women were usually poorly anticoagulated. At present, our program for anticoagulation of female patients is as follows: First, we advise strongly against pregnancy. Second, in the case of a confirmed pregnancy, a strict anticoagulant regimen is established. During the first trimester, Coumadin is discontinued (because of the teratogenic effect), and the patient is put on a regimen of heparin sodium or heparin calcium. During the second trimester, Coumadin is begun again because no teratogenic effect has been described in this period. In the last 2 or 3 months, the patient returns to heparin anticoagulation, because the main risk is anticoagulation of the fetus, which could experience severe hemorrhagic complications during delivery. Because heparin does not cross the placental barrier, this risk is avoided.

Although rheumatic fever is declining in Spain, we are probably now operating on the "last" patients with rheumatic valve disease. Perhaps that is why the surgical risk is higher than before. In general, they are patients in whom the disease process has been long and in whom we often find severe pulmonary vascular disease, atrial fibrillation, and more than one affected valve. Usually they are more than 40 years old, are in functional class III or IV, and have had one or more previous operations.

Endocarditis is a severe complication after valve replacement and requires aggressive treatment. The incidence of endocarditis in our series is 5.4% (19/351), and the majority (47%) of cases were found early in the postoperative period. Six patients did not have reoperation. In 2, this was because good results were obtained with antibiotic therapy; 1 patient refused reoperation, and the other 3 patients were terminally ill at admission and operation was not considered. Thirteen patients did undergo reoperation, and 3 required a second reoperation. We have not had any deaths in the immediate postoperative period of the first reoperation.

In our opinion, mechanical valves are a great advance in valve replacement therapy. Though not yet perfect, they provide satisfactory results. In our experience and that of others [2, 13–15, 28, 29, 30], the Medtronic-Hall valve has proved to be a reliable prosthesis. No structural failures have occurred with these devices. Their durability and wide occluder movement favor fine hemodynamic performance, and, at the same time, they have one of the lowest thromboembolic rates described in the literature. Mild hemolysis was found in almost all patients but was well tolerated. For all these reasons, we consider the Medtronic-Hall valve a prosthesis of choice.

We are grateful to Dr Pifarré for his help in reviewing this paper.

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Clinical Experience With Portable Cardiopulmonary Bypass in Cardiac Arrest Patients

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To evaluate the use of portable cardiopulmonary bypass as a resuscitative tool and its impact on long-term survival of patients in cardiac arrest, we reviewed the results of 32 consecutive patients resuscitated by cardiopulmonary bypass for cardiac arrest or severe hemodynamic compromise at Northwestern Memorial Hospital over a 2-year period. Overall survival was 12.5%. Only 1 (3.4%) of the 29 patients who had cardiac arrest survived and left the hospital. All 3 patients who had severe hemodynamic compromise but not cardiac arrest were long-term survivors. Our study suggests that portable cardiopulmonary support systems used as a resuscitative tool do not prolong the survival of most cardiac arrest patients but may be useful for patients with shock due to mechanical causes and for those with profound hemodynamic compromise due to ischemia or myocardial infarction. Portable heart-lung machines can provide patients with excellent hemodynamic support; however, neurological or cardiac recovery is unlikely once cardiac arrest occurs.

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With the advent of large-bore, thin-walled cannulas and portable heart-lung support machines, cardiopulmonary bypass (CPB) can now be instituted quickly and efficiently in virtually any hospital setting. Portable CPB is a simple and effective system for controlling a patient's circulatory and respiratory functions on an emergency basis until physicians have time to evaluate the cause of the patient's hemodynamic collapse and to initiate further treatment.

The commercially available cardiopulmonary support (CPS) systems are portable units composed of a centrifugal pump, an oxygenator, heater, pump tubing, and venous and arterial cannulas. Because this new technology is portable and easy to apply, cardiothoracic surgeons have renewed their interest in the use of CPB as an emergency resuscitative tool for patients in cardiac arrest. Although this therapy can provide excellent cardiopulmonary resuscitation and support for a variety of patients, previous studies have not clearly shown it to be of benefit to cardiac arrest patients [1–5].

To evaluate the impact of portable CPB on the long-term survival of patients with cardiac arrest, we studied the results in a series of 32 consecutive patients who had cardiac arrest or severe hemodynamic compromise and were resuscitated by emergency CPB at Northwestern University Medical Center from March 1987 through February 1989. Two thirds of the patients subsequently underwent aggressive diagnostic and therapeutic interventions directed at correcting the cause of the cardiac arrest. Our findings form the basis of this report.

Material and Methods

We began using the Bard CPS system (Bard Cardiosurgery Division, C.R. Bard, Billerica, MA) at Northwestern Memorial Hospital in March 1987. Over a 2-year period from March 1987 through February 1989, 32 patients were placed on CPB within a mean time of 9.5 minutes after telephone request for this procedure. Either a nurse trained in CPB or, on occasion, a registered perfusionist assembled, deaired, and primed the system with crystalloid solution. Through a right groin cutdown, an experienced cardiovascular surgeon injected sodium heparin into the femoral veins of these patients and inserted thin-walled, 20F Teflon cannulas into the femoral arteries and veins without gaining proximal or distal control of either vessel (Fig 1). With use of a modified Seldinger technique [6], guidewires and cannulas were inserted as soon as the common femoral artery and vein were identified. When cannulation was complete, the surgeon connected the appropriate bypass pump tubing. Once the bypass equipment was connected to the patient, pump flow was maximized by adjusting the venous cannula (which is longer than the arterial cannula and extends to the right atrium) and by infusing volume. We then decreased ventilation to one breath every 15 to 20 seconds, discontinued cardiopulmonary resuscitation, and defibrillated patients when necessary. Radial or femoral arterial lines were used for monitoring blood pressure in all patients. Swan-Ganz catheters were used for hemodynamic monitoring only in those patients who underwent additional procedures (Table 1). When central venous access was obtained in these patients, we decreased the bypass flow momentarily to prevent air from being sucked into the system. Left ventricular venting was not used.

Thirty-six requests for CPB for cardiac arrest patients

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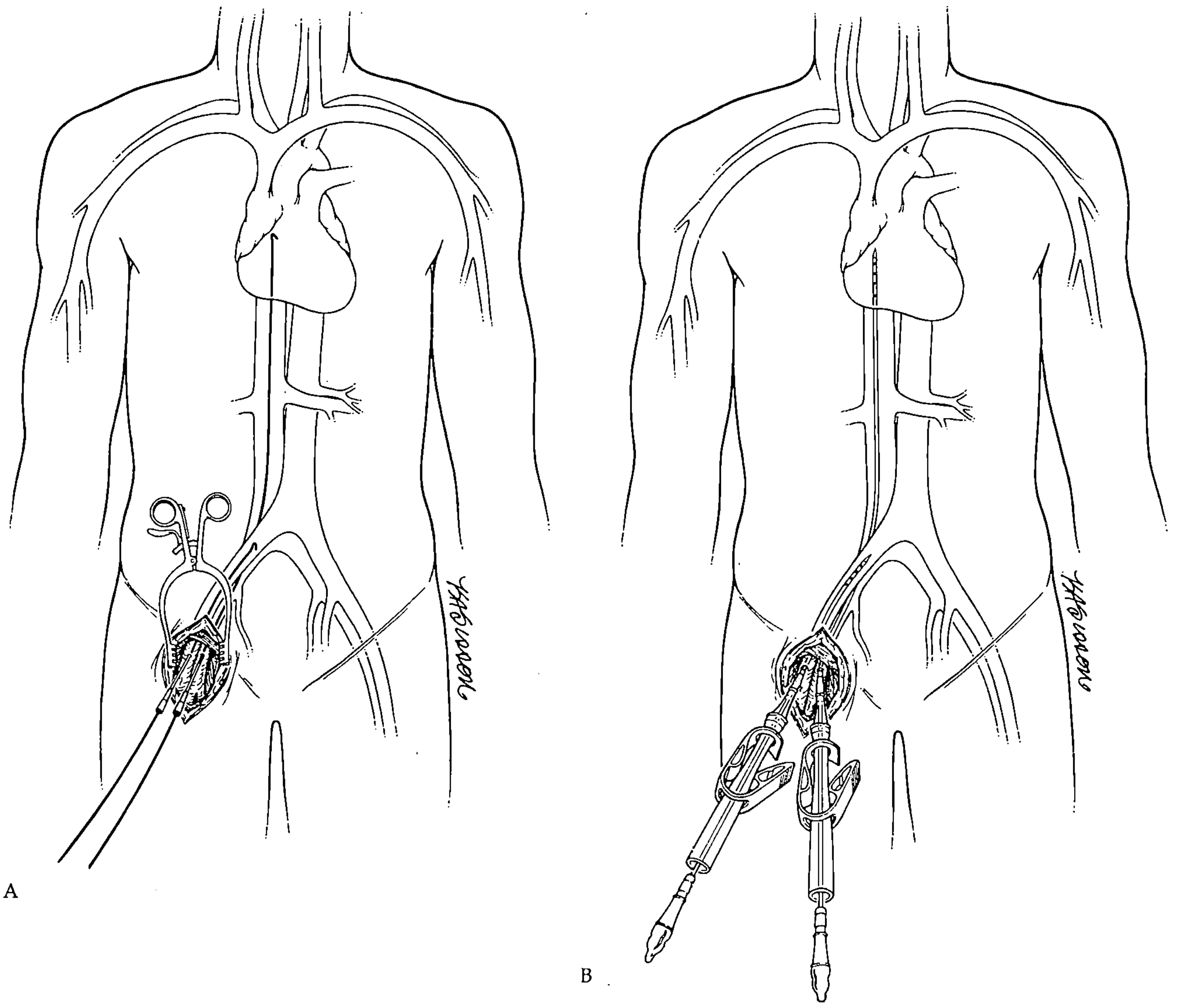

Fig 1. (A) An experienced cardiovascular surgeon performs a right groin cut-down followed by systemic heparinization, 18-gauge femoral venipuncture, and 18-gauge femoral arterial puncture. Guidewires are inserted (0.038, 150 cm). (B) A 20F, 65-cm, thin-walled Teflon cannula is advanced and adjusted with endholes in right atrium.

were made in the 2-year period. Three of the requests were denied by the attending cardiothoracic surgeon. Among the remaining 33 patients, severe bilateral iliofemoral occlusive disease precluded cannulation in 1 patient and difficulties encountered in the use of the cannulas early in the series led to three other failures in instituting the bypass system. The manufacturer provided improved cannulas and guidewires in June 1987, however, and we had no subsequent cannulation difficulties. Ultimately, we were successful in connecting the CPS bypass system to 29 cardiac arrest patients.

Nineteen of these 29 patients (59.0%) had cardiac arrest due to cardiogenic shock caused by ongoing myocardial infarction. In the remaining 10, cardiac arrest was due to a variety of other causes: hypothermia in 2 patients, pulmonary embolus in 2, and amniotic fluid embolus, aortic dissection, hyperkalemia, sepsis, ventricular tachycardia, and unexplained cardiovascular collapse in 1 each (Table 2). The cardiac arrest episodes occurred in an intensive care unit in 9 patients, outside the hospital in 6, in the emergency room in 6, and in an operating room in 5; one episode each occurred in the catheterization laboratory, the radiology suite, and the hospital ward room.

In contrast, 5 additional patients were in profound shock and were placed on bypass using the 20F cannula with conventional bypass equipment. Two of these patients had cardiac arrest, but the other 3 did not. Of the 2 patients who were undergoing radiopulmonary resuscitation, 1 had a reperfusion injury that occurred 15 minutes after a coronary bypass procedure was completed, and the other had a massive myocardial infarction that occurred during a thoracotomy and lobectomy for cancer.

These 5 patients were treated with a CPB system consisting of thin-walled cannulas and a standard roller-pump bypass circuit with gravity drainage. This alternative method was used because 3 of the patients experienced hemodynamic collapse in or near the cardiac surgical suite and the other 2 had right ventricular lacerations that precluded the use of centrifugal pumping.

Results

Cardiopulmonary bypass was used as an emergency resuscitative procedure in 29 patients with cardiac arrest and in another 3 patients in profound shock. For cardiac arrest patients, CPB was instituted in 10 of the 29 patients within 15 minutes of cardiac arrest, in a range of 15 to 30 minutes in another 9 patients, and in 30 minutes or more after cardiac arrest in the remaining 10 patients. Once the telephone request for CPB was made, a mean time of 9.5 minutes was required for the support team to place these patients on bypass (range, 5 to 35 minutes). The mean blood flow achieved on the CPS system was 4.2 L (range, 3.0 to 5.2 L). Patients were maintained on CPS for a mean duration of 2 hours 10 minutes (range, 12 minutes to 6.5 hours). Portable CPB provided good hemodynamic support in all but 1 patient (who had undergone an aortic dissection and was placed inappropriately on the bypass system). In all patients, either ventricular fibrillation spontaneously converted to a more stable rhythm shortly after initiation of CPB (sinus, junctional, or idioventricular) or such a rhythm was easily generated with one or two electrical countershocks.

Nineteen of the 29 cardiac patients (65%) underwent subsequent diagnostic or therapeutic procedures, all of which we performed while the patients were on CPB. Seven patients underwent cardiac catheterization, 2 of whom had percutaneous transluminal coronary angioplasty while on bypass. Cardiac surgical procedures included coronary artery bypass grafting in 6 patients, valve replacement in 2, endocardial resection in 1, and pulmonary artery exploration in 4. Intraaortic balloon counterpulsation was instituted in 5 of the patients. One patient had a centrifugal left ventricular assist device placed after coronary artery bypass grafting and 1 had both a centrifugal right ventricular assist device and a pneumatic left ventricular assist device. The 2 patients who were hypothermic were rewarmed on CPB, and 1 patient with hyperkalemia had dialysis through the arterial and venous bypass lines (Table 1). For patients who required a cardiac operation, full hemodynamic monitoring was instituted and bypass support was converted to right atrial and aortic cannulation with gravity drainage once the patient's chest was opened. The remaining 10 patients were determined to be clinically brain dead, and no further measures were taken.

Table 1. Diagnostic and Therapeutic Interventions During Cardiopulmonary Bypass[a]

Intervention	No. of Patients
None	10
Cardiac catheterization	7
CABG	6
IAB	5
Pulmonary artery exploration	4
Centrifugal VAD	2
Valve replacement	2
PTCA	2
Rewarming	2
Pneumatic VAD	1
Dialysis	1
Endocardial resection	1

[a] Most patients had more than one intervention.

CABG = coronary artery bypass grafting; IAB = intraaortic balloon; PTCA = percutaneous transluminal coronary angioplasty; VAD = ventricular assist device.

Table 2. Cause of Cardiac Arrest

Cause	No. of Patients
Cardiogenic shock	19
Hypothermia	2
Pulmonary embolus	2
Amniotic fluid embolus	1
Aortic dissection	1
Hyperkalemia	1
Unexplained cardiovascular collapse	1
Sepsis	1
Ventricular tachycardia	1

Before initiation of the subsequent procedures, patients had additional invasive monitoring, including Swan-Ganz catheter and arterial line placement. Weaning from portable CPB necessitated accurate measurement of pulmonary capillary wedge pressure, central venous pressure, and arterial pressure. Weaning was accomplished by decreasing pump flow gradually with concomitant hemodynamic observation and measurement of thermodilution cardiac outputs. Patients with adequate hemodynamics at flows of 1 to 1.5 L were then removed from portable CPB. Twenty-two of the 29 cardiac arrest patients could not be removed from CPB despite the aggressive measures shown in Table 1. Only 1 of the 7 patients who were successfully weaned from bypass (a young woman with unexplained cardiovascular collapse during a gynecological procedure) survived cardiac arrest and was able to leave the hospital. Thus, the long-term survival rate among this group of 27 cardiac arrest patients was a mere 3.7%.

Among the 6 short-term (less than a week) survivors of cardiac arrest, 1 patient remained neurologically intact but died of a cardiac arrhythmia 72 hours after being removed from CPB, 2 showed signs of neurological improvement but died of low cardiac output, 1 was believed to be brain dead and subsequently died of ventilatory failure, and 1 died of hemorrhagic shock from retroperitoneal hemorrhage due to a cannula complication that occurred shortly after successful pulmonary embolectomy. The last patient, a young woman with a global reperfusion injury 15 minutes after coronary artery bypass grafting, was placed back on bypass to facilitate placement of a pneumatic left ventricular assist device and centrifugal right ventricular assist device. Even though this patient was neurologically intact and showed signs of substantial recovery of cardiac function, she died 5 days later of low cardiac output and multiorgan system failure shortly after the ventricular assist devices were removed. Her family had denied a request to place her back on circulatory support.

All 5 patients treated with CPS cannulas and conventional bypass equipment had good hemodynamic support, with a mean pump flow of 3.5 L. Two of these patients were placed on bypass because they had sustained right ventricular lacerations while undergoing pericardiectomy. As soon as we placed the venous cannulas in these patients, massive volume infusion was possible and we were able to complete the pericardiectomy with the patient on CPB. Both patients survived and left the hospital in good condition. The other 3 patients had hemodynamic collapse in or immediately adjacent to the operating room where conventional bypass equipment was more readily available than the CPS system.

In the entire series of 32 patients who were resuscitated by portable CPB over a 2-year period, only 1 of the 29 patients who had cardiac arrest survived (3.4%), whereas all 3 patients who underwent emergency CPB and did not suffer cardiac arrest survived (100%).

Comment

Portable CPB is a powerful resuscitative tool that can be used on an emergency basis almost anywhere in a hospital by an experienced surgical team. Currently available systems are safe and easy to assemble. The femoral arteriotomy created by the cannula can easily be closed primarily. Major vascular complications are slight; in our experience, only 1 patient had a major vascular complication (retroperitoneal hemorrhage from a cannula perforation) and it is not certain whether the cannula or the insertion technique actually caused the complication.

Because the mortality rates of cardiogenic shock and cardiac arrest are so high [7–11], we were very aggressive in our early application of this new technology. We considered all patients with witnessed cardiac arrest who had received cardiopulmonary resuscitation immediately to be candidates for continued resuscitation with CPB. Decisions concerning further diagnosis and treatment could then be made in a controlled setting.

We were able to provide this service in our hospital on a 24-hour basis. When the team was consulted, preparations for CPB were started even while the history was being obtained. Although 23 of the 29 patients had cardiac arrest in the hospital and even though CPB was instituted on the average less than 10 minutes after the request for it was made, only 1 patient with cardiac arrest survived more than 1 week. On the other hand, as expected, CPB proved an extremely efficacious method of resuscitating patients who had profound hemodynamic compromise but did not actually suffer a cardiac arrest. All 3 such patients in this series, including 1 with a massive myocardial infarction, survived, left the hospital, and are well more than 6 months after discharge.

An obvious question that arises from this experience and one that poses an ethical dilemma is whether these patients had too much or too little resuscitation. Cardiopulmonary bypass cannot be continued indefinitely, and current FDA regulations allow use of the CPS equipment for a maximum of 6 hours. Should we, as physicians, continue to support the cardiovascular systems of patients with possible brain death when this would involve major surgical procedures and expensive ventricular assist devices? Will the brains of these patients recover even when they have had absolutely no return of brainstem reflexes after 2 to 4 hours of excellent hemodynamic support? Because we do not know the answers to these questions, and because patient consent for CPB was implied in the first place, we could not recommend further diagnostic or therapeutic measures to the families of 10 of our patients who appeared to have both cardiac and brain death. These patients were slowly separated from the bypass circuit, had no evidence of cardiac ejection, and died.

It is entirely possible that both cardiac and neurological activity might resume in these patients if they were supported for a longer period of time. For example, venting the left ventricle may facilitate cardiac recovery; although we did not note progressive ventricular distention in our patients, 2 of them who had left main coronary occlusions and who underwent cardiac catheterization had no evidence of cardiac mechanical activity despite the presence of spontaneous cardiac rhythms. This angiographic correlate of electromechanical dissociation was improved in 1 patient by left main coronary angioplasty, but the patient never had cardiac ejection sufficient to sustain life. Twelve hours later, the patient had diffuse hemorrhage from prolonged CPB and no neurological function and died. This patient is a typical example of the problems involved with resuscitating the cardiovascular system but not the patient. Ideally, a multicenter trial of resuscitation with CPB will be undertaken, and patients such as this one will be randomized to various treatment arms after informed consent is obtained from the family.

In the meantime, we currently use CPB as a resuscitative tool in patients with a mechanical cause for shock (such as ventricular injury during repeat sternotomy) and for patients who are profoundly ischemic but who have not yet had a cardiac arrest. Patients who have an out-of-hospital arrest are no longer routinely considered, nor are those who have cardiac arrest in the hospital but who had cardiopulmonary resuscitation for more than 30 minutes.

The thin-walled cannulas themselves can be extremely useful, and good bypass flows can be achieved even with gravity drainage. For this reason, we now place angiocatheters in both the femoral artery and vein of all our patients undergoing redo cardiac operations. The CPS cannulas are in the room, the pump is primed, and the perfusionist is present. Surgical exposure of the femoral vessels is therefore unnecessary for rapid institution of femoral bypass.

As with most new technologies, the exact role of portable CPB systems will take some time to clarify. We are not discouraged by our early results, however, because 4 of the 32 patients who would have died without this intervention did survive (including one young woman with a cardiac arrest). In the future, we will try to apply this technology earlier in the course of treatment. We also hope to be part of a multicenter trial organized to define not only patient selection but also the degree and length of cardiac resuscitation that should be used in cardiac arrest patients.

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Pericardial Window: Mechanisms of Efficacy

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Although the term implies a persistent communication through which fluid might drain, how a *pericardial window* works is not clear. We believe that the mechanism of success is not a window but rather fusion of the epicardium to the pericardium with obliteration of the potential space. To evaluate this, we studied 28 patients, all of whom underwent a subxiphoid pericardial window procedure with tube drainage maintained until output was minimal. There were no operative deaths, and 26 patients (92.9%) obtained permanent relief. Postoperative echocardiograms demonstrated thickening of the pericardium/epicardium and obliteration of the pericardial space. Autopsy performed on 4 patients who died of their underlying malignancy confirmed this fusion, which begins as an inflammatory process. A subxiphoid pericardial window relieves effusions with a low operative mortality and good long-term success (92.9%, 26 of 28). This success is dependent on the inflammatory fusion of the epicardium to pericardium and not maintenance of a window. Tube decompression should be maintained until fluid output is minimal to allow apposition and fusion of the two surfaces.

(Ann Thorac Surg 1990;50:442–5)

Although operations for effusive pericardial disease have been performed since the original description of a subxiphoid pericardiotomy by Baron Larrey in 1829 [1], controversy persists regarding the optimum surgical approach [2–5]. Pericardial window is one frequently performed operation, but some surgeons have been so disappointed with their results that they have abandoned the operation in favor of total pericardiectomy [4, 5]. Other experiences with pericardial window have been much more satisfactory [6–11]. Because a window can be created by several approaches, this discrepancy in results suggests that not all techniques achieve equivalent outcomes. The concept of a pericardial window for effusive disease implies a free and persistent communication between the pericardium and either the pleural cavity or the subcutaneous tissues into which fluid drains or is absorbed. However, it is unlikely that a true window can remain and accomplish this goal. We postulated that the key to therapy was fusion of the epicardium and pericardium to obliterate any potential space and that an important aspect in managing patients toward that end is adequate and continued tube decompression. To examine this theory, we reviewed the clinical course of patients who had undergone a subxiphoid pericardial window procedure.

Material and Methods

Twenty-eight patients who had a subxiphoid pericardial window performed by us were included in this study. The patients ranged in age from 25 to 65 years; 19 were women and 9 were men. The underlying diagnosis was carcinoma in 24 patients and renal failure in 4. Twenty-six of the 28 patients had symptomatic pericardial effusions with varying degrees of tamponade. The other 2 patients, both with carcinoma, were operated on for diagnosis and drainage of large effusions but had no symptoms directly related to the presence of fluid.

Each patient underwent the pericardial window by the subxiphoid route under general anesthesia as previously described [10]. A short vertical incision was made overlying the xiphoid process, through the uppermost aspect of the linea alba. A 3 × 3-cm swath of pericardium was excised, and all fluid was drained. Careful digital, visual and, occasionally, endoscopic examination of the pericardium was performed, and all adhesions were lysed. Argyle drainage tubes, placed anterior and posterior to the heart, were maintained on suction by waterseal drainage systems until drainage was less than 50 mL in 24 hours; this usually occurred within 3 to 5 days after operation. The fluid obtained was analyzed cytologically, chemically, and bacteriologically, and the excised pericardium was submitted for gross and microscopic examination.

Preoperative and postoperative echocardiograms, both two-dimensional and M-mode, were obtained in all patients (Hewlett Packard 77020A Ultrasound System, 2.25-MHz transducer). Preoperative studies were obtained within a week of operation. At least one postoperative examination was obtained in all patients between 1 and 2 months after operation; some had multiple examinations.

Autopsies were performed on 4 patients who died between 6 weeks and 8 months after operation. All these patients had carcinoma as their primary diagnosis. The heart and pericardial cavity were examined completely, and both gross and histological appearances were defined.

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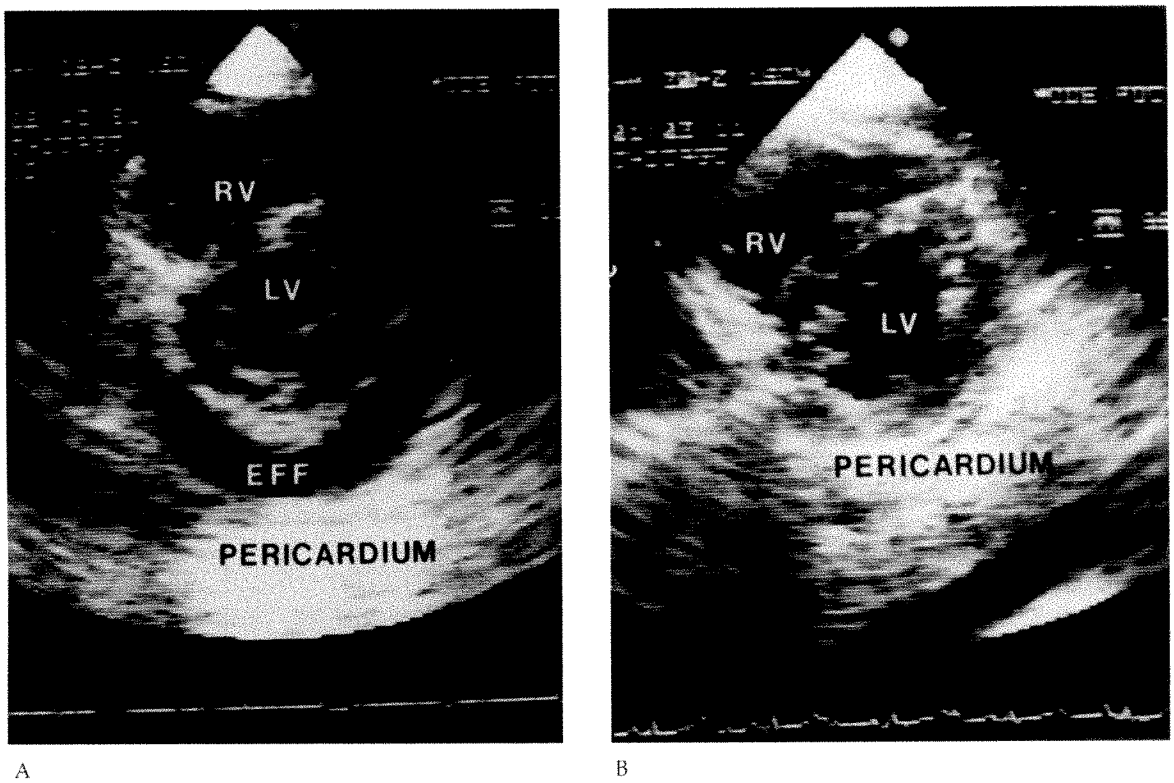

Fig 1. (A) Preoperative two-dimensional echocardiogram shows a large posterior pericardial effusion (EFF). *(B) Postoperative two-dimensional echocardiogram shows fluid removal, obliteration of the pericardial space, and a thickened, fused pericardium to epicardium.* (LV = *left ventricle;* RV = *right ventricle.)*

Results

Preoperative echocardiograms demonstrated the presence of a moderate to large pericardial effusion in all patients, with impairment of right ventricular filling identified in some (Fig 1A). At operation, the amount of fluid removed in the 24 cancer patients averaged 433 mL; in the 4 uremic patients, it averaged 878 mL. There were no operative deaths. All patients with malignancy eventually died of their underlying disease, with an average survival of 120 days (range, 38 to 331 days). All patients with uremic effusions were alive at the end of the study. Overall, 26 of 28 patients remained free of recurrent effusions (92.9%). Two cancer patients (7.1%) had recurrent pericardial tamponade due to hemorrhage at 6 and 9 weeks after operation. Reoperation by the subxiphoid approach was successfully performed in 1 of these patients; the other patients died of the hemorrhage.

The postoperative echocardiograms demonstrated at most a minimal amount of fluid in the pericardium and a thickened, fused epicardium/pericardium in all patients (Fig 1B). Similarly, the autopsy findings showed no free pericardial fluid. The pericardium was diffusely adherent to the epicardium, with fibrinous adhesions and obliteration of the pericardial space by a reactive pericarditis (Fig 2). The window itself was filled with fibrinous debris, and the mesothelial surfaces had not reapproximated. The histological appearance showed fusion of the epicardium and pericardium into a single tissue plane (Figs 3–5).

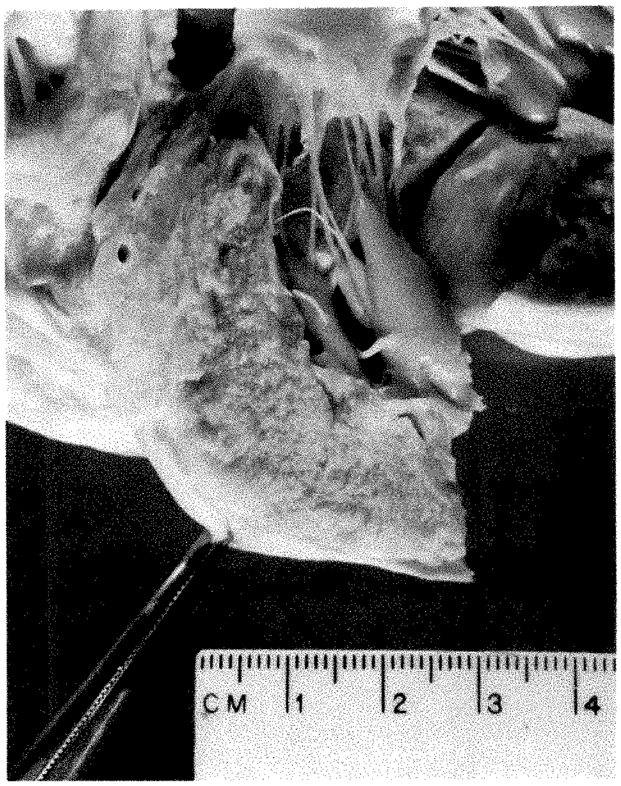

Fig 2. Postmortem examination in a patient who had undergone pericardial window 8 months earlier. Cut section through left ventricle shows fusion of pericardium (forceps) to epicardium.

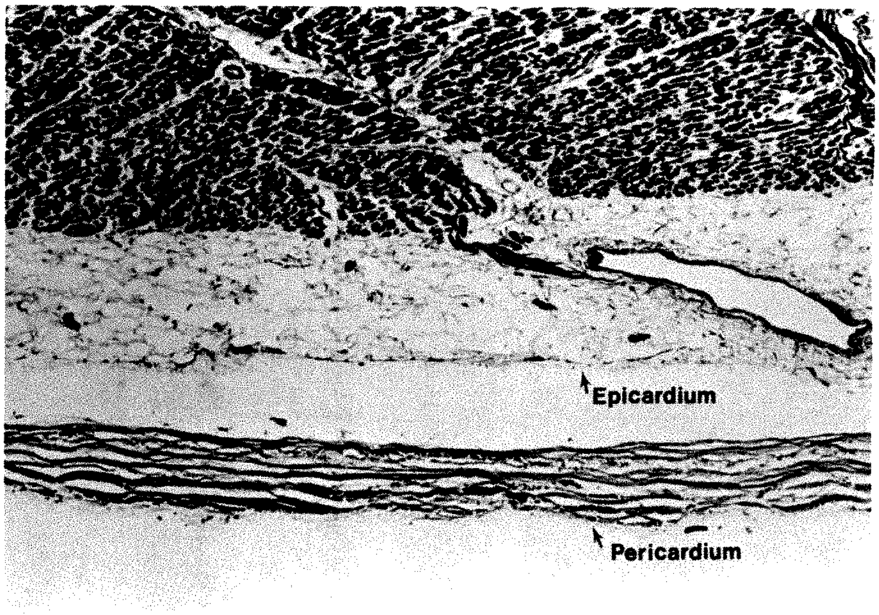

Fig 3. Normal histological preparation shows the pericardium, potential pericardial space, and epicardium with a medium-sized coronary artery.

Comment

The term *window*, in reference to pericardial disease, was first used by Williams and Soutter [12] in their description of an anterior thoracotomy for creation of a communication between the pericardium and left pleural space in which the pericardium was actually stitched to the lung to ensure permanent drainage. The inferior, left subcostal, or subxiphoid approach to the pericardium was originally described by the Napoleonic surgeon Baron Larrey in 1829

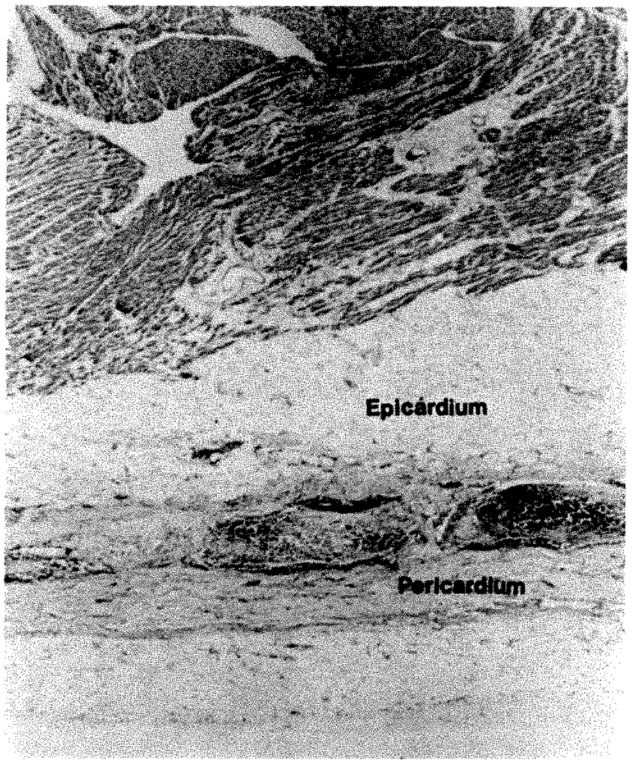

Fig 4. Early postmortem examination (6 weeks) shows a reactive pericarditis. The pericardial space is filled with an inflammatory exudate.

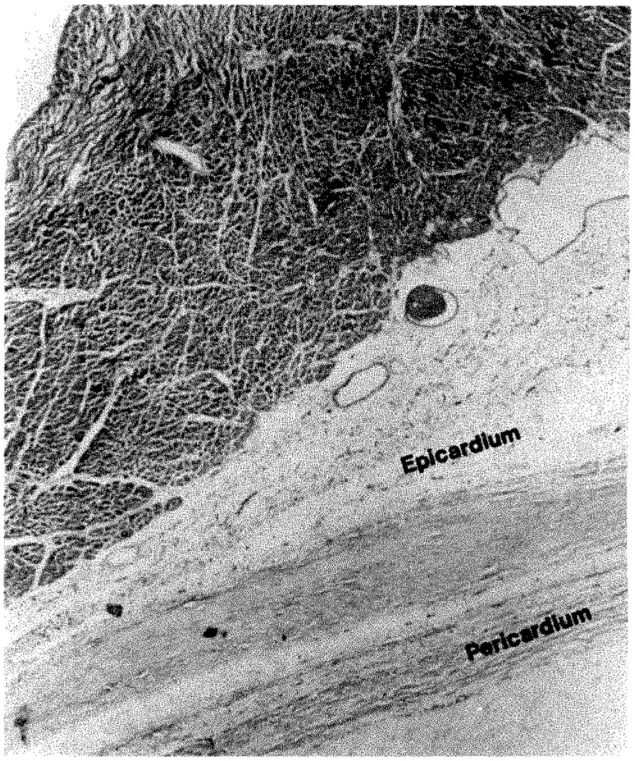

Fig 5. Late postmortem examination (8 months) shows the fibrous stroma that fuses pericardium to epicardium.

[1] and subsequently was used by Ogle and Allingham in 1900 [13]. Not until 1970, however, did Fontanelle and colleagues [14] apply the term *window* to the subxiphoid approach.

The acute safety and efficacy of pericardial windows in the setting of cardiac tamponade is well documented [11, 15]. The long-term benefits of a window procedure have been questioned, however [2–4]. Our enthusiasm for the subxiphoid pericardial window is based on experience demonstrating that the procedure can be performed safely and that it provides definitive diagnostic and therapeutic results for all forms of effusive disease [10]. It has the advantage of being a short and relatively small-scale operation that can be performed using only local anesthetic if necessary. This must be taken into serious consideration because these patients often have a fatal malignancy as their primary problem and a limited life expectancy [16, 17].

Our data suggest that therapeutic efficacy of windows depends on two major factors. First, it is important to achieve initial complete drainage of the pericardial fluid. An equally crucial factor for long-term success, however, is continued pericardial drainage until fibrinous adhesions between the epicardium and the pericardium can begin. This process results from the inflammatory response to either trauma, the operation, or the underlying pathological process. This eventually leads to obliteration of the pericardial space by fibrinous adhesions such as those that are routinely found after open heart operations. Postoperative echocardiograms and autopsy material show that success results from establishing this fusion. Continued decompression of the pericardial space must be maintained until adherence of the epicardium and pericardium begins, as signaled by minimal drainage through the tubes. At this time, which is rarely more than a few days after operation, the tubes can be removed. Instillation of sclerosing agents is not necessary. When this technique is used, results are comparable with those obtained with a total pericardiectomy, a considerably more extensive operation.

Although none of our patients with carcinoma survived to 1 year, each dying of the primary disease process, only two effusions recurred and all patients obtained symptomatic relief. No recurrent effusion or constrictive pericarditis has developed in any patient with benign disease. We believe that the subxiphoid approach with pericardiotomy and tube drainage to effect fusion is the surgical approach of choice, although select patients may require or benefit from total pericardiectomy. Surgeons performing operations for patients with effusive disease must have as their goal either fusion of the parietal and visceral pericardium or resection of the entire pericardium. A simple window will close and does not represent effective therapy for this disorder.

We acknowledge JoAnn Bauer for help in manuscript preparation.

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Iatrogenic Paraesophageal Hiatus Hernia

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Between January 1970 and January 1990, 101 patients with paraesophageal hiatus hernias were operated on at the Lahey Clinic Medical Center. Thirteen patients had hernias that were identified as being iatrogenic in origin, a prevalence of 13%. Ten hernias were secondary to antireflux procedures, and esophagomyotomy, esophagogastrectomy, and placement of an Angelchik prosthesis accounted for one case each. Symptoms did not differ substantially from those of patients with primary hernias. Incarceration occurred in 2 patients, but neither sustained strangulation. The pathogenesis was most frequently disruption of a previous hiatal closure. Other etiological factors included disruption of the phrenoesophageal membrane by operative dissection, postoperative gastric dilatation, and failure to recognize esophageal shortening or an existing hiatal defect. Abdominal repair was usually possible, but 3 patients required thoracotomy for reduction. There has been one known recurrence during a median follow-up of 41 months.

(Ann Thorac Surg 1990;50:446–9)

Operations involving the esophageal hiatus and distal esophagus can cause paraesophageal hernias. Although this complication is rare, it carries the same serious implications as a primary hernia and requires prompt surgical treatment. The iatrogenic paraesophageal hiatus hernia presents therapeutic challenges because of previous surgical therapy, and treatment must be individualized. This summary of the Lahey Clinic experience with iatrogenic paraesophageal hiatus hernia during a 20-year period identifies etiological factors, describes methods of prevention and repair, and analyzes the results of surgical treatment.

Material and Methods

Thirteen patients with paraesophageal hiatus hernia secondary to previous esophageal operations were identified in a review of records of all patients seen at the Lahey Clinic Medical Center between January 1970 and January 1990 (Table 1). The hernias in these patients represented 13% of the 101 paraesophageal hernias repaired during this period. The 7 patients whose initial procedures were performed at the Lahey Clinic represented 0.7% of the 963 operations on the distal esophagus (excluding primary paraesophageal hiatus hernia repairs) during this same period. Two patients were referred for treatment of recurrent iatrogenic paraesophageal hiatus hernia due to prior fundoplication.

The most common symptom was postprandial epigastric or substernal pain. Only 2 patients were asymptomatic. In all patients a portion of the stomach, usually the fundus, had herniated into the chest alongside the esophagus. Incarceration occurred in 2 patients, but neither sustained strangulation.

Cause

The pathogenesis of the hernias was difficult to ascertain with certainty but could be identified presumptively in most patients. Eight hernias secondary to fundoplication appeared to result from disruption of the previous hiatal closure. A wide hiatal defect was discovered in these patients at reoperation (patients 1, 3, 6, 8–11, and 13). In 2 of these patients, substantial esophageal shortening was associated with the hiatal disruption, and a third patient had early postoperative gastric dilatation that appeared to contribute to the gastric herniation. In 2 patients, a major hiatal defect may have been unrecognized at the time of the original operation (patients 5 and 12). Too extensive a hiatal enlargement during esophagogastrectomy led to one hernia (patient 7). A Penrose drain in the hiatus anterior to the esophagus led to a defect in that area in patient 4. No cause was obvious in patient 2.

Diagnosis

The diagnosis of paraesophageal hernia was made in all patients by an upper gastrointestinal contrast study (Fig 1). Six of the 11 patients who had had previous antireflux operations underwent manometry before hernia repair, and all 6 had normal to high pressure in the lower esophageal sphincter.

Surgical Treatment

Hiatal closure was performed with heavy interrupted nonabsorbable sutures placed anterior to the esophagus, posterior to the esophagus, or both depending on the location of the defect in relation to the gastroesophageal junction. Three patients underwent revision of a previous fundoplication: 1 because of gas-bloat syndrome and 2

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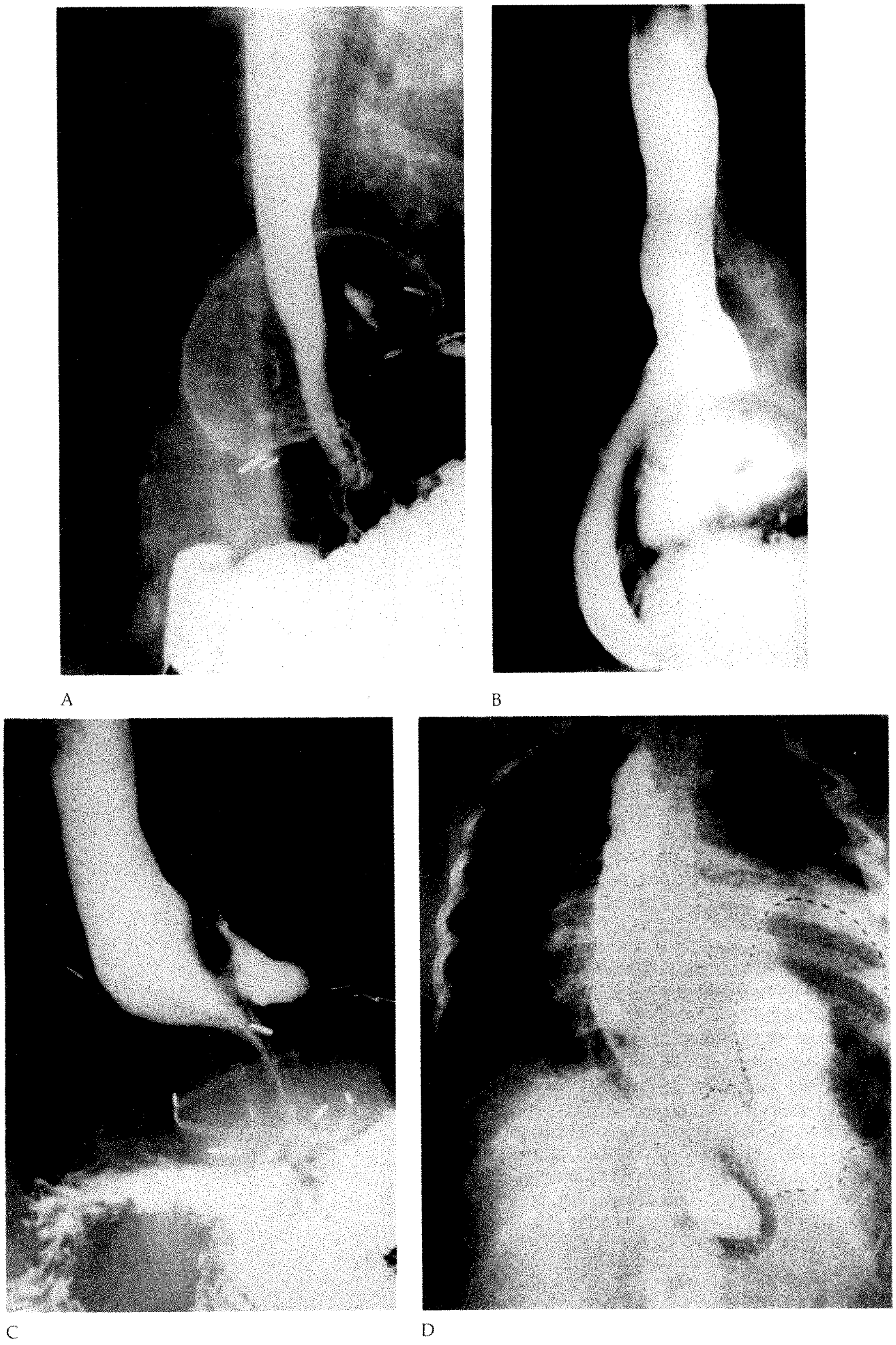

Fig 1. Barium swallow upper gastrointestinal films show iatrogenic paraesophageal hiatus hernias after (A) Nissen and (B) uncut Collis-Nissen fundoplications, (C) insertion of an Angelchik prosthesis, and (D) transthoracic esophagomyotomy for achalasia (broken line = *outline of stomach). (Figure 1D is reprinted from [1] by permission of the publishers, Butterworth & Co.©.)*

Table 1. Patients With Iatrogenic Paraesophageal Hiatus Hernia, 1970–1990

Patient No.	Age (y)	Sex	Previous Operation	Symptoms	Interval to Repair	Surgical Treatment
1	35	M	Nissen	Pain	26 mo	Abdominal repair, Nissen redone
2	63	M	Uncut Collis-Nissen	None	12 mo	Thoracic repair, uncut Collis-Nissen redone
3	56	M	Collis-Nissen	Pain	5 mo	Thoracic repair, Marlex mesh closure
4	53	F	Nissen	Pain	48 mo	Abdominal repair
5	53	F	Esophagomyotomy	Pain, heartburn, dysphagia	6 d	Abdominal repair
6	44	M	Nissen	None	70 mo	Abdominal repair
7	58	M	Esophagogastrectomy	Nausea, emesis	3 mo	Thoracic repair
8	44	M	Nissen	Pain	8 mo	Abdominal repair
9	39	M	Nissen	Pain	14 mo	Abdominal repair
10	31	M	Nissen	Pain, regurgitation	72 mo	Abdominal repair
11	42	M	Nissen	Pain	156 mo	Abdominal repair, Nissen redone
12	53	M	Angelchik prosthesis	Pain, dysphagia	35 mo	Abdominal repair, Angelchik removed
13	31	M	Nissen	Dysphagia, early satiety	2 mo	Abdominal repair, gastrostomy

because the fundoplication had been dismantled during dissection of the hernia. Intraoperative manometry was performed in 3 patients. One patient underwent pyloromyotomy because of concern about possible vagal injury. To prevent recurrence of the hernia, suturing of the stomach to the hiatal edges was performed in 1 patient (patient 7), and a gastrostomy tube was inserted in another (patient 13).

Results

There were no operative deaths. Two patients were lost to follow-up. There was one recurrence (9.1%) with a median follow-up of 41 months (range, 1 to 150 months). Functional results of surgical treatment of the original conditions were good or excellent in 8 patients and fair in 1 patient. A poor result occurred in 2 patients: 1 had recurrence of the iatrogenic paraesophageal hiatus hernia (patient 10), and the other required eventual posterior gastropexy for intractable reflux symptoms after removal of an Angelchik prosthesis (patient 12).

Comment

Iatrogenic paraesophageal hiatus hernia is an unusual complication of an esophageal operation, but it does not differ substantially from the more common primary paraesophageal hernia in either clinical presentation or potential for strangulation and infarction [1], and it should be repaired promptly after diagnosis.

The treatment of any iatrogenic problem clearly begins with prevention. Snug hiatal closure at the time of the antireflux operation is essential and can be facilitated by the insertion of a large esophageal dilator before the crural sutures are tied to prevent overtightening. A shortened esophagus can lead to upward traction on the antireflux repair and should be corrected by adequate esophageal mobilization or by a Collis gastroplasty. During transthoracic esophagomyotomy, excessive traction on the esophagus or dissection around the hiatus can disrupt the phrenoesophageal membrane and should be avoided [1, 2]. However, routine hiatal closure and reinforcement of the phrenoesophageal attachments, as advocated by some [3], does not seem necessary when there is no radiographic or operative evidence of a hiatal defect. Enlargement of the hiatus during esophagogastrectomy should permit unconstricted passage of the stomach or intestine without overenlargement. The edges of the hiatus can be sutured to the stomach or intestine to prevent the development of a hernia [4].

Clinical and manometric evaluation, both preoperatively and intraoperatively, identify patients who need revision of the primary procedure. The choice of incision is influenced by the previous surgical approach and the anticipated need for revision; however, a transabdominal approach is generally preferable. Complete exposure of the hiatus is necessary to permit secure repair. An especially large and scarred hiatus could require closure with a prosthetic patch if the edges cannot be approximated without undue tension, although this was necessary in only 1 patient. It should be avoided if possible in view of the hazards of erosion.

Routine use of gastrostomy to prevent recurrence of paraesophageal hernias [5] has not often been possible in our patients with iatrogenic paraesophageal hiatus hernia because of numerous gastric adhesions. Extensive mobilization usually does not seem warranted because the recurrence rate without gastrostomy is low.

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Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1993 may begin the recertification process in 1991. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1991. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Variations Within the Fibrous Skeleton and Ventricular Outflow Tracts in Tetralogy of Fallot

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We studied 20 hearts with tetralogy of Fallot with particular reference to the morphology of the fibrous continuity between the aortic and atrioventricular valves and of the ventricular outflow tracts. The extent of valvar fibrous continuity varied with the degree of aortic override, with the extent of the perimembranous ventricular septal defect opening between the ventricular inlets, and with the development of the ventriculoinfundibular fold. This, when fused with the septomarginal trabeculation, produced discontinuity between the leaflets of the tricuspid valve and the continuous leaflets of the aortic and mitral valves, as well as a muscular posteroinferior rim to the defect. Rotation of the aortic root ranged through 119 degrees. Aortic override varied from 33% to 94%, with 35% of these hearts having more than half of the aortic circumference connected to the right ventricle. The pulmonary valves had three leaflets in 50%, two leaflets in 45%, and four leaflets in one (5%). All hearts had two main coronary arterial orifices, 45% of which were atypical in location. One heart displayed a transmural course of the left coronary artery arising from the nonfacing sinus. By measurement, the subpulmonary length was, on average, roughly 50% greater than the subaortic length, and, when the selected hearts were sectioned, much of the subpulmonary infundibulum was found to be composed of free-standing musculature rather than true outlet septum. The proportion of total right ventricular length represented by the infundibulum was 0.31 ± 0.07, confirming that, compared with that of normal hearts, the narrowed infundibulum in tetralogy is longer rather than shorter.

(Ann Thorac Surg 1990;50:450–7)

The tetralogy of abnormal anatomical features as originally described by Fallot has subsequently been shown to exhibit considerable variation in specific morphology despite the unity of a single diagnosis. The variations have been well documented by several investigators. Thus, Lev and Eckner [1] highlighted the clinical significance of the variations within the setting of cyanotic and acyanotic cases. Other investigators focused on more subtle differences. Goor and co-workers [2] described variation in the fibrous skeleton, noting the rotational variation of the aortic orifice in relation to the lines of the atrial septum and the midpoint of the aortic leaflet of the mitral valve. A subsequent study by Becker and colleagues [3], incorporating detailed geometric measurements, showed lengthening of the narrowed subpulmonary infundibulum in comparison with that of the normal heart and also confirmed the variation in rotation of the arterial axes noted by Goor and co-workers [2]. The morphogenetic significance underlying these variations is still not clearly understood. Defects in septation and rotation of the developing outflow tracts remain the basis of current thought [3, 4] despite continuing claims for "lack of conal growth" [5]. We, therefore, performed further detailed morphological examination of the fibrous skeleton and the structures making up the abnormal ventricular outflow tracts, hoping that further clarification of the variations within these subsystems might lead to better understanding of the developmental anomalies they represent and the surgical stratagems required for their correction.

Material and Methods

Twenty hearts from patients with tetralogy of Fallot were selected from the cardiopathological collection of the National Heart and Lung Institute, Brompton Hospital, London, England. The hearts were examined to determine precisely the variation in the morphology of fibrous continuity between the leaflets of the aortic and the atrioventricular valves, rotational variation within the axis of the great arterial trunks, the degree of override of the aortic orifice relative to the ventricular septum, the anatomy of the leaflets of the pulmonary valve, the arrangement of the coronary arterial orifices, the precise structure of the subpulmonary infundibulum and particularly the septum separating it from the subaortic outflow tract, the ratio of the infundibular length to the overall right ventricular length, and the presence of membranous flaps or pseudoflaps related to the posteroinferior margin of the ventricular septal defect.

Selection of specimens was based primarily on their maximal preservation to permit accurate examination of these features in the presence or absence of operative or

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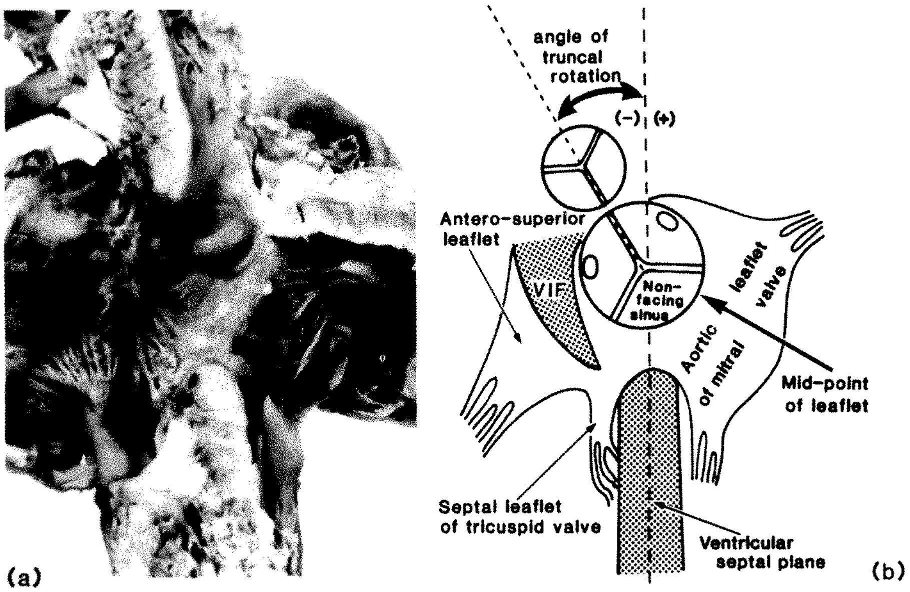

Fig 1. The heart viewed from the ventricular aspect in the short axis (compare with Fig 3). (a) Heart 6 sectioned through the long axis of the ventricular septum shows the relationships of the leaflets of the aortic valve to the ventricular septal crest, the tricuspid valve, and the aortic (anterior) leaflet of the mitral valve. The right ventricular outflow tract and pulmonary valve are obscured by the superiorly reflected ventricular wall. (b) Schematic representation of this heart with labeled components for comparison with those in Figure 3. (VIF = ventriculoinfundibular fold.)

postmortem alteration. Hearts were excluded if such alterations, when present, resulted in excessive distortion or destruction of the outlet septum, pulmonary ventriculoarterial junction, or ventricular septum, although four hearts were included in morphological study despite postmortem alteration of the infundibulum and right ventricular apices that prevented accurate measurements of these areas. Specimens of tetralogy with pulmonary atresia were excluded.

The variations in fibrous continuity of the valvar leaflets were represented diagrammatically (Fig 1). The orientation of the axis of the great arterial trunks was taken in reference to the projection of the ventricular septum relative to the overriding aortic valve. Measurements in degrees of rotation were expressed, with 0 degrees being in the plane of the ventricular septum and positive values representing clockwise rotation as viewed from the ventricular aspect. Aortic override was represented as a percentage of the circumference of the aortic valvar leaflets supported by and connected to the right ventricular structures. The extent of the structures separating the subaortic and subpulmonary outflow tracts was examined initially by measuring the distances from the crest of the outlet septum to the nearest point of attachment of the leaflets of the aortic and pulmonary valves. This was expressed as a relationship using the length of the subaortic component as the denominator (Fig 2). The ratio of the overall infundibular length to right ventricular length was obtained in the manner of the determinations used by Becker and colleagues [3]. This involved the additional measurement of length from the superior point of the pulmonary valvar attachment to the crest of the outlet septum and thence to the right ventricular apex. The infundibular length was then divided by the combined lengths (total right ventricular length), thus representing the proportionate contribution of the infundibulum to right ventricular length. This ratio was then correlated

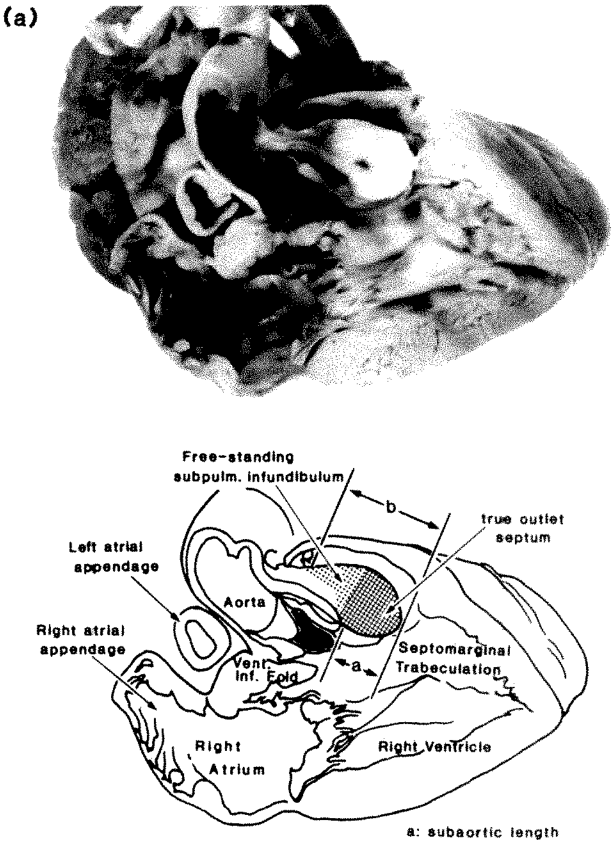

Fig 2. Sectioned heart showing the measurements taken to quantitate the extent of the outlet septum. (a) Heart 16, showing the sectioned subpulmonary and subaortic outflow tracts seen from the right ventricular aspect. The muscular posteroinferior rim of the ventricular septal defect in this heart is also seen to advantage in this section, along with the juxtaposed left atrial appendage. (b) Illustration of the heart shows the anatomic nature of the structures and the measurements taken for quantitation.

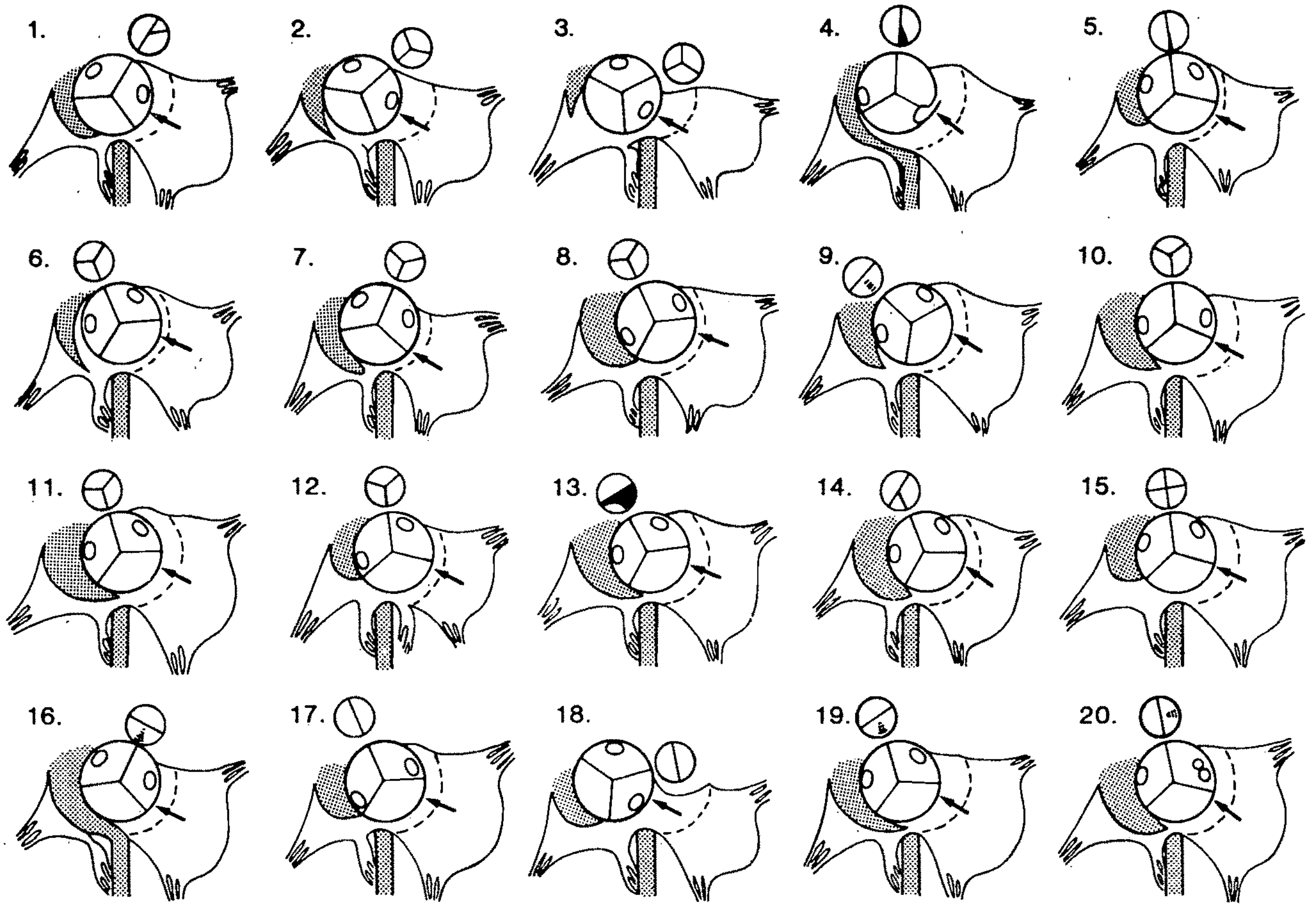

Fig 3. Morphology of the fibrous skeletons and ventricular outflow tracts of the 20 hearts within this study. Representation is from the ventricular aspect in the short axis and compares with the diagram shown in Fig 1b.

with the values obtained in normal specimens as published by Becker and colleagues [3], and the statistical significance of the comparison was determined using Student's *t* test. After measurement, representative hearts were sectioned longitudinally through the area separating the subarterial outflow tracts and examined to determine the part that separated the outflow tracts one from the other (the outlet septum) and the part of the apparently septal aspect of the subpulmonary infundibulum that, in reality, separated the inside from the outside of the heart (free-standing infundibulum) (Fig 2).

Results

A schematic representation of the relationships of the arterial and atrioventricular valves as seen from the ventricular aspect in the short axis of all 20 hearts is shown in Figure 3.

Aortic–Atrioventricular Valvar Fibrous Continuity

In all hearts, the aortic valve was in fibrous continuity with the aortic (anterior) leaflet of the mitral valve. Marked variation was noted in the arrangement of the aortic orifice, as judged by the projection of the midpoint of the mitral leaflet onto the aortic valve. Fibrous continuity of the aortic and tricuspid valves varied in relation to the development of the ventriculoinfundibular fold as well as with regard to the morphology of the posteroinferior margin of the ventricular septal defect. In this respect, there was fibrous continuity between the leaflets of aortic, mitral, and tricuspid valves in the posteroinferior margin of 18 of the defects. This is the criterion we use for labeling the defect as perimembranous (Fig 4a). The extent of fibrous continuity between the aortic valve and anterosuperior leaflet of the tricuspid valve was inversely related to increased development of the ventriculoinfundibular fold. This varied from extensive continuity along the attachment of the anterosuperior tricuspid leaflet in one heart, through various intermediate stages in 17 hearts, to complete discontinuity between the leaflets of the aortic and tricuspid valves in two hearts. The latter situation existed owing to fusion of the ventriculoinfundibular fold with the posterior limb of the septomarginal trabeculation, giving a muscular posteroinferior rim to the defect, which thus was no longer perimembranous (Fig 4b). In four of the hearts in which the defect was perimembranous, it also excavated into the inlet septum such that there was additional fibrous continuity between the leaflets of the aortic valve and the septal (in addition to the anterosuperior) leaflet of the tricuspid valve. An

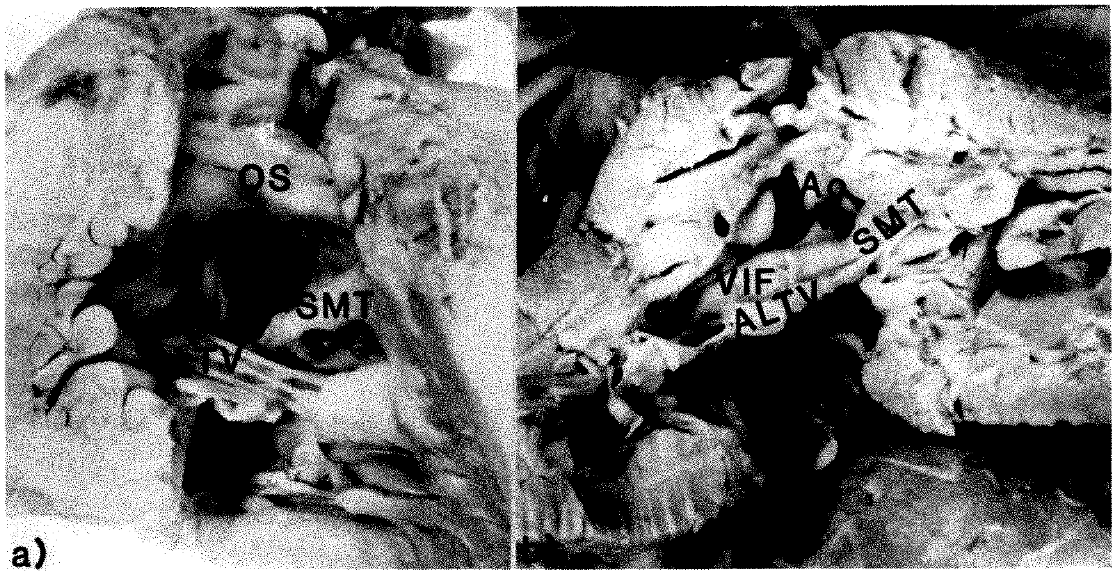

Fig 4. Comparison of examples of perimembranous and muscular ventricular septal defects. (a) Heart 17 with the posteroinferior rim of the ventricular septal defect formed by fibrous continuity between the leaflets of the aortic and tricuspid valves as seen from the right ventricular aspect (perimembranous defect). The septal defect is bordered by the hypertrophied outlet septum; superiorly, the stenosed right ventricular outflow tract is evident. (b) Heart 4 shows fusion of the ventriculoinfundibular fold and septomarginal trabeculation, creating a muscular posteroinferior rim to the ventricular septal defect. The anterosuperior tricuspid leaflet spans the muscular rim in this view; the rim produces fibrous discontinuity between the leaflets of the tricuspid valve and those of both the aortic and mitral valves. (AoV = *aortic valve;* ALTV = *anterosuperior leaflet of tricuspid valve;* OS = *outlet septum;* SMT = *septomarginal trabeculation;* VIF = *ventriculoinfundibular fold.)*

abnormal attachment of the leaflets of the tricuspid valve to the outlet septum was noted in two of these hearts with inlet extension of the perimembranous ventricular septal defect (Fig 5).

Great Arterial Orientation

Rotational orientation of the great arterial trunks varied through 119 degrees (range, −45 to +74 degrees; mean, 2.37 ± 31.86 degrees; median, −5.75 degrees).

Aortic Override

The degree of aortic override in the hearts studied ranged from 33% to 94% (mean, 56.9% ± 16.05%; median, 50%). Seven hearts (35%) had greater than 50% override and thus represent tetralogy of Fallot with double-outlet ventriculoarterial connection from the right ventricle. Plotting aortic override against truncal rotation, the values showed approximate proportionality at the extremes, with greatest variability within the broad region of equal override between the ventricles (−45 to +26 degrees) (Fig 6).

Arrangement of the Pulmonary Leaflets

In eight hearts (40%), the anticipated arrangement of three leaflets was present although the valve was itself stenotic. An abnormal pattern having three leaflets was noted in two hearts (10%; hearts 1 and 14): one large leaflet had "bicuspid"orientation, and the other, markedly smaller leaflets were separated unequally by a commissure. Nine hearts (45%) exhibited valves with two leaflets. Four of the valves displayed commissural orientation in alignment with the adjoining aortic commissure, whereas the remainder were oriented at right angles to it. A rudimentary mural raphe was present in four of the valves with two leaflets. One "bicuspid"valve had a single rudimentary leaflet (heart 13), whereas another had one leaflet that was incomplete (heart 4). One valve had four leaflets (heart 15). A commissure (or rudimentary related structure) was present opposite the commissure between the two coronary leaflets of the aortic valve in 18 of the 20 hearts. In the remainder, there was commissural mismatch of approximately 90 degrees in one (heart 18), and in the other the main stem of the left coronary artery took a transmural course to originate from the nonfacing sinus of the aorta (heart 4).

Arrangement of Coronary Orifices

In 11 of the hearts (55%), the openings of both the right and left coronary arteries were situated centrally within their respective sinuses of Valsalva at or below the line of attachment of the commissures. In the other nine hearts, the orifices of the coronary arteries were displaced toward the commissures. One left coronary artery possessed a double orifice (heart 20), and the orifices of both right and left arteries were displaced high out of the sinuses in another. One heart displayed an intramural course of the main stem of the left coronary artery such that it originated from the nonfacing (or posterior) sinus of Valsalva adjacent to the commissure (heart 4; Figs 3, 7). Despite these slight variations in position and the extreme variations noted in truncal rotation, the left coronary artery originated within or at the limit of the region of aortic–mitral fibrous continuity in all specimens.

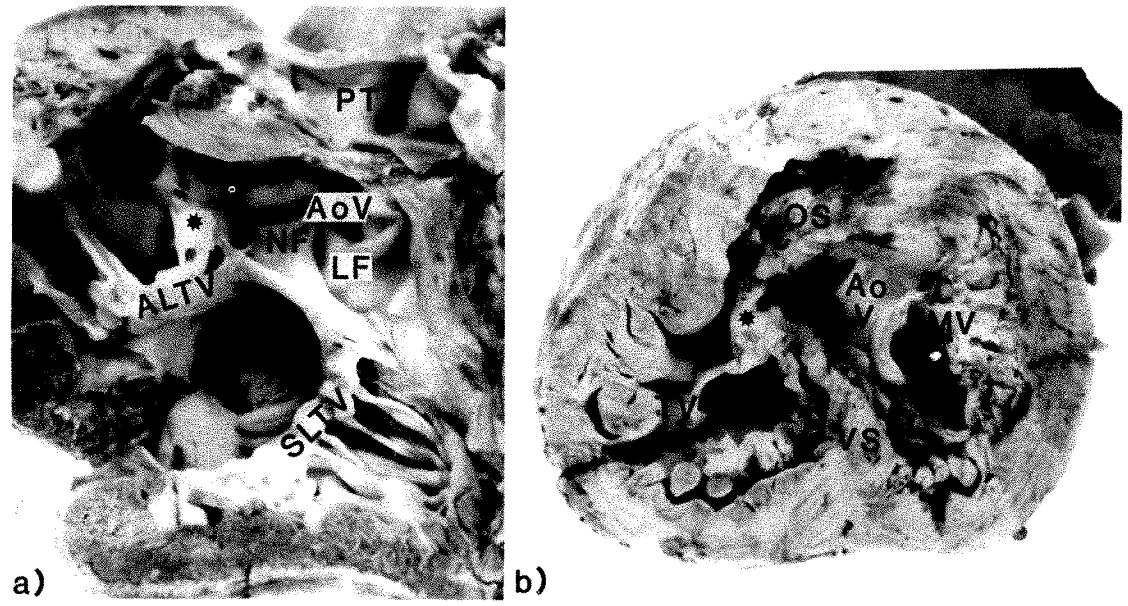

Fig 5. Heart 2: (a) The outlet septum was sectioned near its septal insertion and retracted laterally with the right ventricular free wall. The heart is viewed from the right ventricular aspect. Extension of the perimembranous ventricular septal defect so that it opens between the inlets yields a broad area of fibrous continuity between the leaflets of the aortic and tricuspid valves. The abnormal attachment of tricuspid chordal apparatus (*) to the parietal insertion of the outlet septum is also evident. (b) Cross-section through the ventricular chambers of the same heart shows the valvar orientations as seen from the ventricular aspect. The anterior displacement of the outlet septum is apparent, along with the abnormal attachments of the tricuspid valve extending to its parietal insertion (*). (AoV = *aortic valve;* ALTV = *anterosuperior leaflet of tricuspid valve;* LF = *left-hand facing leaflet of aortic valve;* NF = *nonfacing leaflet of aortic valve;* SLTV = *septal leaflet of tricuspid valve;* PT = *pulmonary trunk;* OS = *outlet septum;* VS = *ventricular septum;* MV = *mitral valve;* TV = *tricuspid valve.)*

Outlet Septum

The mean proportion of subpulmonary length to subaortic length along the outlet septum was 1.54 ± 0.41 (range, 1.0 to 3.0; n = 19). With the subpulmonary aspect of the outlet septum averaging roughly one and a half times the length of the subaortic aspect, a substantial proportion of the purported "outlet septum" was suspected to be composed of free-standing subpulmonary infundibular musculature. Sectioning through the septum confirmed that a substantial proportion of this structure was indeed free-standing infundibulum, with only a small component contributed by what is commonly known as the outlet septum (Figs 2, 8). The most distal part of the "septal" component of the subpulmonary infundibulum in the

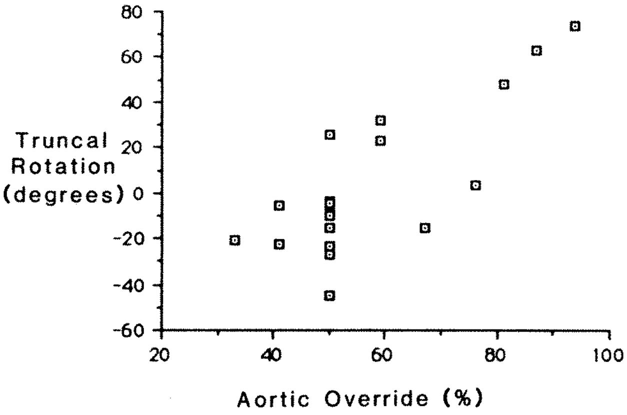

Fig 6. Plot of percentage of aortic override against degrees of truncal rotation.

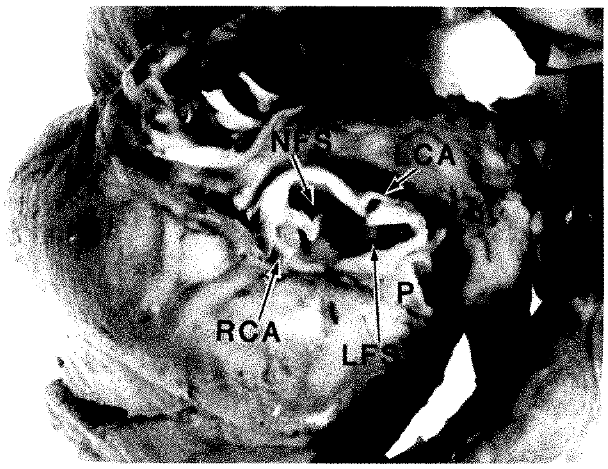

Fig 7. Photograph of heart 4 taken from the superior aspect after sectioning and retraction of the aorta just above the commissural attachments of the aortic valve. The pulmonary trunk was also removed. The transmural course of the main stem of the left coronary artery is evident, with its orifice situated just within the nonfacing sinus and adjacent to its commissure. The orifice of the right coronary artery is evident in normal position within the right-hand facing sinus of Valsalva. (LCA = *left coronary artery;* RCA = *right coronary artery;* NFS = *nonfacing sinus;* LFS = *left-hand facing sinus;* PT = *pulmonary trunk.)*

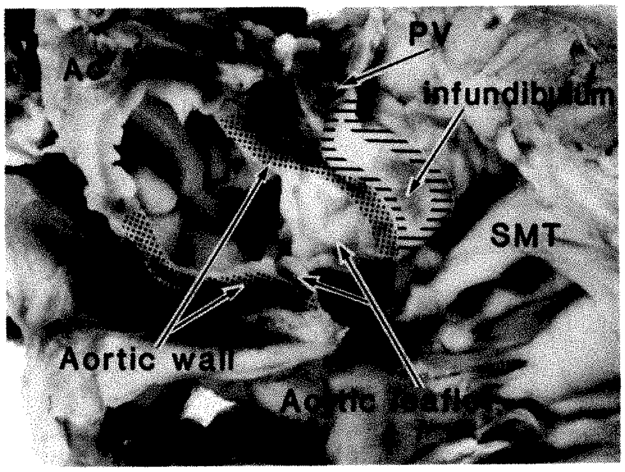

*Fig 8. Heart 17 after sectioning of the outlet septum. The extent of the aortic wall and valvar attachments is evident, along with those of the pulmonary trunk and valve. The hypertrophied subpulmonary musculature is predominantly composed of free-standing infundibulum. (*Ao *= aorta;* PV *= pulmonary valve;* SMT *= septomarginal trabeculation.)*

sectioned specimens separated the subpulmonary outlet from a tissue plane between the aorta and the pulmonary trunk. The mean ratio of infundibular to right ventricular length was 0.31 ± 0.07 (range, 0.22 to 0.46; n = 17) in this series. This was somewhat less than the value obtained in the 14 specimens with tetralogy reported by Becker and colleagues [3] (0.36 ± 0.08; range, 0.21–0.50) but is greater than that of the 10 normal specimens in their series (0.28 ± 0.03; range, 0.23 to 0.34). Statistical analysis of our data in comparison with these normal values indicated that our findings of increased proportional infundibular length as compared with normal hearts approached statistical significance without being conclusive ($p = 0.076$), although the broader spectrum of proportions we observed more closely approximated those observed in hearts with tetralogy in the series of Becker and colleagues [3].

Flaps/Pseudoflaps

Membranous flaps or pseudoflaps related to the ventricular septal defect were present in eight specimens. Six were membranous flaps and one was a pseudoflap; one heart had both structures. The pseudoflaps were produced by reduplication of tricuspid valvar tissue, and fenestration was present in both of them to varying degree.

Comment

The variation within the singular morphological entity of tetralogy of Fallot is well established [1, 6], a variation endorsed still further by this study. The underlying aberration is that of abnormal septation of the developing outlet component of the ventricular mass along with defective incorporation of the aorta into the left ventricle; this feature yields the superocephalad deviation of the outlet septum and overriding of the aortic orifice [2, 3]. In addition, the arrangement of the leaflets of the aortic valve shows considerable rotational variation in terms of the fibrous continuity achieved with the aortic (anterior) leaflet of the mitral valve. This was well described by Goor and co-workers [2], who documented aortic "dextroposition" in relation to the lines subtended by the atrial septum and the midpoint of the aortic leaflet of the mitral valve. This variation is further reflected in terms of the extent of fibrous continuity observed between the leaflets of the aortic and tricuspid valves and also between those of the mitral and tricuspid valves. The latter feature is marked when the septal defect extends into the inlet of the right ventricle, but is completely lacking when the defect possesses a muscular posteroinferior rim.

Although many factors come into play during formation of the fibrous skeleton and in the achievement of valvar fibrous continuity, one major feature must be the attenuation and obliteration of the muscular inner heart curvature. Early in development, muscular tissue separates the leaflets of the developing arterial and atrioventricular valves; it is apparent in the roof of the developing left and right ventricles even after closure of the embryonic interventricular communication [7]. This musculature persists to separate the leaflets of the tricuspid and pulmonary valves in the right ventricle. In contrast, it is usually attenuated during development of the roof of the left ventricle so that fibrous continuity is established between the leaflets of the aortic and mitral valves. Even in the normal heart, aortic-tricuspid valvar continuity also exists through the fibrous substance of the membranous septum. This fibrous continuity is evident in hearts with tetralogy, and its extent is closely interrelated with the degree of connection of the aortic valve within the right ventricle. With the greater proximity of the aortic and tricuspid valves produced by increased aortic override, fibrous continuity is enhanced, whereas such continuity at this level becomes limited by persistence of the interposed ventriculoinfundibular fold. As indicated, however, these are not the only factors involved, and other forces are undoubtedly of significance.

The concept of abnormal septation of the outlet component and abnormal incorporation of its aortic component within the left ventricle continues to be supported by this investigation as a crucial mechanism in the morphogenesis of tetralogy of Fallot. Studies of embryonic and fetal material [8, 9] have shown that in animals this results from abnormal positioning of the ridges that divide the outlet component of the heart tube. Although the concept of rotation of the outlet component during development relative to the atrioventricular junction remains controversial, the anatomical evidence of a 119-degree spectrum of rotation observed in our material approximates the 110 to 150 degrees of rotation postulated from studies of human embryos [10, 11]. This suggests the interesting possibility that the abnormal hearts reflect the range from the nonrotated to the relatively normally rotated outlet component, with the independent variables of septation, rotation, and absorption of the inner heart curvature exerting their effects on rightward position of the aorta and the associated morphology of aortic-tricuspid-mitral valvar fibrous continuity. Within this series of tetralogy of Fallot, all specimens showed fibrous continuity between the leaflets of the aortic and mitral valves; this is not, however, an essential feature of tetralogy. As we have discussed, the cardinal features of tetralogy are the abnormal septation of the ventricular outflow tracts at the expense of the subpulmonary component and the abnormal attachment of the leaflets of the aortic valve within the right ventricle. This feature can coexist with muscular discontinuity between the leaflets of the aortic and mitral valves, as exemplified by the case described by Dickinson and associates [12]. This consideration bears closely on the relationship between tetralogy of Fallot and "classic" double-outlet right ventricle with bilateral infundibular musculature. These entities are distinguished on the basis of their overall morphology, not simply by the presence or absence of fibrous continuity between the leaflets of the aortic and mitral valves. The coexistence of a classic example of tetralogy and almost complete double-outlet ventriculoarterial connection is seen in heart 18, which has the greatest extent of rightward position of the aorta and the smallest amount of aortic-mitral fibrous continuity, the latter barely spanning the area of the left facing leaflet of the aortic valve. The morphology of the infundibular structures is independent of the ventriculoarterial connection. This independence is further emphasized by the fact that, rarely, normal hearts can exist with discontinuity between the leaflets of the aortic and mitral valves [13].

Our observations concerning the structures separating the subaortic and subpulmonary outlets are important in that free-standing subpulmonary infundibular musculature was shown to be a crucial component of this supposedly septal region. Our macroscopic sections reveal the proximity of the leaflets of the aortic valve to the crest of the outlet septum as well as the extensive area of separation of the great arterial trunks by epicardial fat, this tissue plane interposing between the aortic wall and the subpulmonary infundibular musculature. This finding reflects recent observations in the normal heart concerning the limited extent of the so-called outlet septum [14], together with embryologic investigations supporting such anatomical studies [15]. It also has surgical importance, as it supports the concern over risks inherent in attempts at resection of the hypertrophied body of the outlet septum as in the conotruncal repair described by Kurosawa and associates [16]. It is apparent that the aortic valvar apparatus can be endangered in such maneuvers, and the risk of such resection becoming extracardiac is obvious. It should also be noted that the subpulmonary infundibulum exhibited considerable length in all the specimens we studied. The previous investigation of Becker and colleagues [3] showed, by measurement, that the infundibulum in tetralogy of Fallot in their series of 14 hearts was significantly longer than those in normal hearts when compared with the overall length of the right ventricle. Although we were unable to duplicate their finding of significant elongation of the infundibulum exactly, statistical comparison of our measurements in the abnormal hearts with their measurements of normal specimens showed that the infundibular length was certainly not shorter than normal; rather, in the hearts with tetralogy it was slightly elongated. Despite the significant differences shown by statistical analysis in the study of Becker and colleagues [3] Van Praagh [17] still maintains, without presenting supporting evidence, that the subpulmonary infundibulum is short in tetralogy of Fallot, arguing that it is unwise to "generalize" from the study of Becker and colleagues [3]. The findings in this study, based on 17 other hearts, continue to support the concept of Becker and colleagues [3], as did the much more extensive investigation of Anderson and co-workers [6]. Although occasionally the subpulmonary infundibulum may be short in tetralogy of Fallot, it is a mistake to maintain that it is "short in all dimensions" [17].

The variations noted in arrangements of the coronary arterial orifices are among the most minor of such abnormalities (if, indeed, they are abnormal at all!). Most are unlikely to have clinical or surgical significance. Regardless of arterial orientation, however, the left coronary artery always originated from the aortic sinus within or at the limit of the region of aortic–mitral fibrous continuity even at the extremes of rotational variability. The mural transcommissural course of the main stem of the left coronary artery in one heart is also unlikely to be of clinical significance, but its origin from the nonfacing sinus of the aorta is of considerable interest. Well-documented examples of origin of a coronary artery from the nonfacing aortic sinus are exceedingly rare. Indeed, we know of no such examples. Although not important in the setting of tetralogy of Fallot, such a finding would have major significance if replicated in a patient with complete transposition, particularly if an arterial switch procedure was contemplated as the means of surgical correction.

Membranous flaps and pseudoflap structures related to the posteroinferior margins of the ventricular septal defects were relatively common findings in this series, although not present in all hearts as suggested by Kurosawa and associates [18]. Pseudoflaps were also somewhat less common in our selected hearts than in the overall series reported by Suzuki and co-workers [19]. Membranous flaps are remnants of the interventricular component of the membranous septum lying posteriorly in the defect roughly in the plane of the muscular septum. Pseudoflaps are derived from the leaflets of the tricuspid valve. In the present study, the pseudoflaps extended to achieve attachment to the outlet septum in two of the hearts that bore perimembranous defects extending to the inlet of the right ventricle. Caution may be warranted in use of such tissue during surgical repair, as fenestrations may be present and could result in inadequate closure of the defect with residual interventricular shunting. In relation to the other anomalies noted within these hearts, the heart with right juxtaposition of the atrial appendages was important not only in bearing a muscular septal defect characterized by fibrous discontinuity between the leaflets of the tricuspid valve and the continuous leaflets of the aortic and mitral valves, but also, according to a recent review of the literature by Seo and colleagues [20], in appearing to be a previously unreported morphological constellation.

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Malignant Fibrous Histiocytoma of the Trachea

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A 17-year-old woman was admitted with malignant fibrous histiocytoma of the cervical trachea. The very rare occurrence of malignancy in this tumor at that location and its unusual presentation, misdiagnosis, and surgical management in the face of near-total tracheal occlusion make its reporting worthwhile.

(Ann Thorac Surg 1990;50:458–9)

Malignant fibrous histiocytoma of the trachea is an extremely rare tumor [1]. This report presents a case of malignant fibrous histiocytoma of the cervical trachea and its surgical management.

A 17-year-old woman was referred to Emory University Hospital on November 7, 1988, after having been treated for asthmalike symptoms during the past year. The patient complained of recent increase in shortness of breath and wheezing with chest wall retraction. Tomograms of the trachea showed a large mass in the lower cervical trachea (Fig 1). A computed tomographic scan of the neck and chest showed an endotracheal mass at the thoracic inlet arising from the right lateral tracheal wall and occluding approximately 80% of the tracheal lumen (Fig 2).

On November 8, 1988, under isoflurane anesthesia and without muscle relaxants, the patient underwent bronchoscopy that showed a large polypoid tumor almost completely obstructing the tracheal lumen 4 cm distal to the vocal cords. The bronchoscope could not be passed beyond the tumor, and no attempt was made to perform a biopsy on it for fear of bleeding. An adequate airway could not be maintained.

The patient was prepared and draped. Using a low-neck collar incision, a tracheostomy was performed just distal to the tumor, and a sterile anode tube was introduced into the lower trachea. The trachea was mobilized anteriorly down to the carina and posteriorly off the esophagus using finger dissection. No dissection was carried out laterally except at the resection site to protect the blood supply. A segment of trachea comprising five rings was resected with primary end-to-end anastomosis using interrupted 3-0 PDS sutures with the knots tied on the outside.

The patient had an uneventful postoperative course and was discharged on the 13th postoperative day. A second bronchoscopy on January 3, 1990, 14 months postoperatively, showed no evidence of tumor recurrence.

The tracheal mass was polypoid, soft, tan-white, and homogeneous and measured 1.5 × 1.5 × 1.3 cm. The mass eroded the tracheal wall through the mucosa. Histologically, the neoplasm was composed of spindle cells arranged in a storiform pattern with scattered Touton giant cells and areas of hyalinization. There was moderate nuclear pleomorphism, but mitoses were rare (Fig 3). Immunohistochemistry and electron microscopy supported the light microscopic classification of the lesion as a fibrohistiocytic neoplasm. The neoplasm gave positive reactions with antibodies to vimetin, actin, S-100 protein, and HAM-56, whereas antibodies for epithelial markers gave negative reactions (cytokeratin and epithelial membrane antigen). The final pathological diagnosis was consistent with low-grade malignant fibrous histiocytoma and was confirmed on review of the case by the Armed Forces Institute of Pathology.

Comment

Malignant fibrous histiocytoma is a mesenchymal tumor first recognized by O'Brien and Stout [2] in 1964. Earlier, Kauffman and Stout [3] hypothesized that the histiocyte was a facultative fibroblast that gave rise to a variety of histological patterns. Malignant fibrous histiocytoma is the most common malignant neoplasm of the soft tissues and most commonly occurs in the extremities and trunk [4], but it has also been reported in the lung and mediastinum [5].

In 1981, Blitzer and co-workers [6] reviewed the occurrences of malignant fibrous histiocytoma in the head and neck region. They reported 87 cases. The most affected sites in decreasing order were the maxillary sinus, the mandible, and the larynx. They noted that malignant fibrous histiocytoma of the larynx was a biologically aggressive tumor often recurring after surgical resection and metastasizing to different organs (lung, brain, heart, kidney, liver, spleen, skin, musculoskeletal, subcutaneous tissues, regional lymph nodes).

In contrast to the more aggressive behavior of laryngeal malignant fibrous histiocytoma, the behavior of the neoplasm in the tracheal location appears to be benign. Gonzalez-Compora and associates [7] reviewed the literature and found 6 reported cases, all of which were benign. They concluded that fibrous histiocytoma of the trachea is a benign tumor. They also noted that the majority of tumors occurred in young adult females, were located in the upper third of the trachea, and were polypoid in nature. The patients were most commonly

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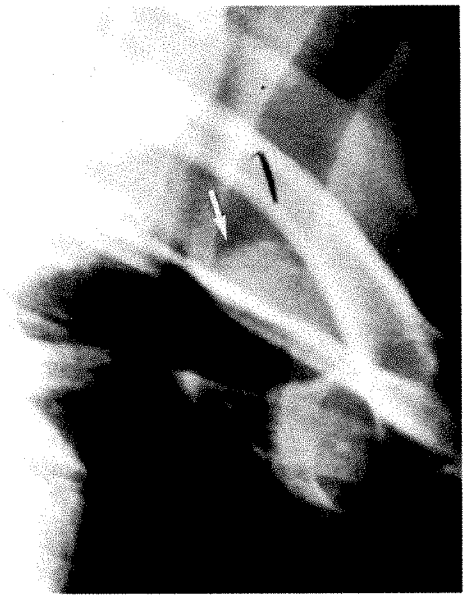

Fig 1. Tomogram showing a large endotracheal mass.

seen with hemoptysis, progressive dyspnea, and stridor. In spite of the tumor's histologically benign features, recurrences after local resection were frequent. The review noted that fibrohistiocytic tumors of the trachea were in marked contrast to the fibrohistiocytic tumors seen at other levels of the respiratory tract, primarily those of the larynx and lung, in which the malignant form and distant metastases were more frequent.

The only previously reported case of malignant fibrous histiocytoma of the trachea was by Louie and co-workers [1] in 1983. Bronchoscopic laser therapy was used, but the tumor recurred rapidly despite adjuvant chemotherapy, and the patient died 3 months after her hospital admission.

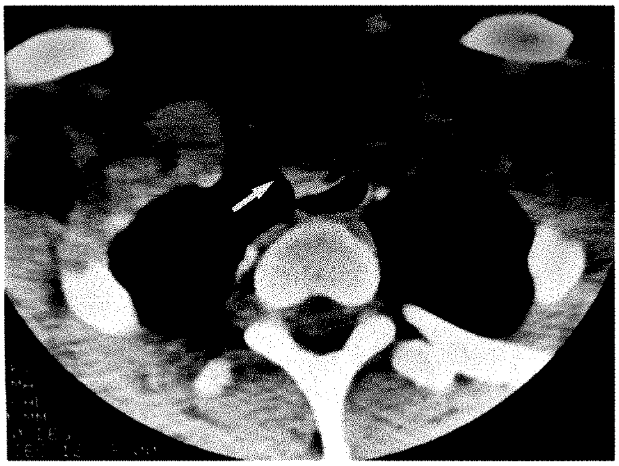

Fig 2. Computed tomographic scan shows tumor nearly occluding tracheal lumen (arrow).

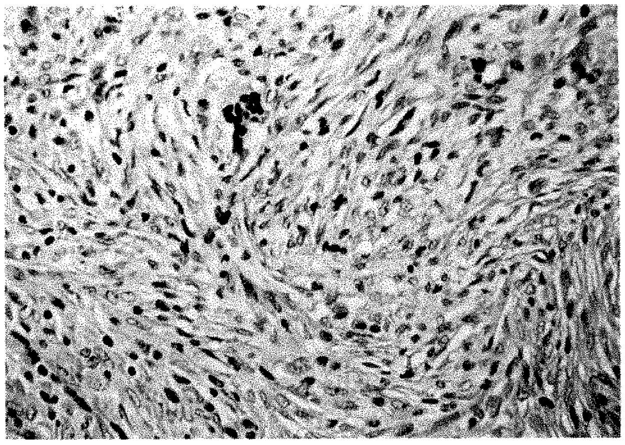

Fig 3. Representative section of tracheal neoplasm showing closely packed fibrohistiocytic cells arranged in storiform pattern. Giant cell is present in this field. (Hemotoxylin and eosin, ×40 before 50% reduction.)

The treatment of malignant fibrous histiocytoma of the trachea should be aggressive wide local excision. This approach is shared by most reviews of fibrous histiocytic tumors. Radiation therapy has limited efficacy as the tumors are considered radioresistant. Leite [8] reported a 33% response rate for malignant fibrous histiocytomas treated with multiple chemotherapeutic agents for a mean duration of 10 months. Kearney and colleagues [9], however, have found the benefits of chemotherapy to be diverse and ineffective.

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Systemic Venous Aneurysms

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A case of superior vena cava aneurysm combined with aneurysm of the left innominate vein is presented. For the diagnosis, it is important not only to apply imaging techniques such as superior vena caval angiography, radioisotopic angiography, and computed tomographic scans but also to have a concept of this entity in mind.

(Ann Thorac Surg 1990;50:460–2)

In a review by Kelly and co-workers [1], almost 10% of intrathoracic mass lesions were reported to be of vascular origin. However, most vascular lesions are systemic arterial aneurysms. On the other hand, systemic venous lesions are so rare that their clinical significance is not known. We treated a patient with a superior vena caval aneurysm combined with an aneurysm of the left innominate vein.

A 13-year-old boy was admitted to the National Himeji Hospital on August 22, 1985, for further evaluation of an abnormal shadow on his chest roentgenogram. He had been healthy since birth. Results of physical examination and laboratory tests were all normal. A posteroanterior chest roentgenogram showed a marked shift of the cardiac shadow to the left (Fig 1). A computed tomographic chest scan showed a dilated superior vena cava (SVC) and a left anterior mediastinal mass that was so enhanced by contrast medium that a vascular lesion or a vascular-rich tumor was suspected (Fig 2). Venous angiograms demonstrated fusiform dilatation of the SVC and saccular dilatation of the left innominate vein (Fig 3). Venous pressure was 4 mm Hg in the innominate vein, the SVC, and the saccular aneurysm of the left innominate vein. The diagnosis was fusiform aneurysm of the SVC combined with saccular aneurysm of the left innominate vein. According to clinical reports, fusiform aneurysm of the SVC is never complicated by rupture or thrombus formation, and the prognosis is good. However, surgical resection of the saccular aneurysm was planned because of the possibility of thrombus formation resulting in pulmonary embolism.

The operation was performed on September 11, 1985. Median sternotomy combined with fifth intercostal thoracotomy was selected as the approach into the anterior mediastinum. The left lung seemed hypoplastic without collapse, and the aneurysm of the left innominate vein was located above the lung. The aneurysm was 5 × 4 cm; three dilated vessels, presumably the second, third, and fourth intercostal veins, drained into it. The inferior end of the aneurysm extended down along the chest wall becoming thinner and finally disappearing. There was no connection with the coronary sinus, which ruled out a left SVC (Fig 4). The wall of the dilated SVC looked normal, and no clot was detected inside the SVC. The three dilated intercostal veins were isolated and divided, and the inferior end of the innominate vein aneurysm was isolated and divided for the next operative procedure. Next, a vascular clamp was placed at the superior end of the aneurysm, which was resected peripheral to the clamp. Gentle handling was used to prevent possible lung embolism. The proximal end of the resection line was closed with 5-0 Prolene suture (Ethicon). An old clot was found at the inferior end of the resected aneurysm. Pathological examination showed normal architecture of the systemic vein, which ruled out inflammation or any structural defect.

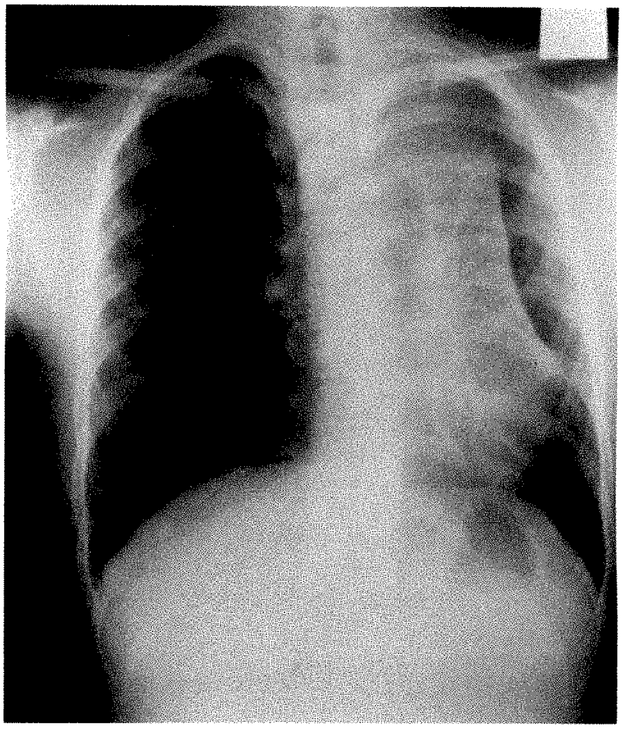

Fig 1. Posteroanterior chest roentgenogram shows a marked shift of the cardiac shadow to the left.

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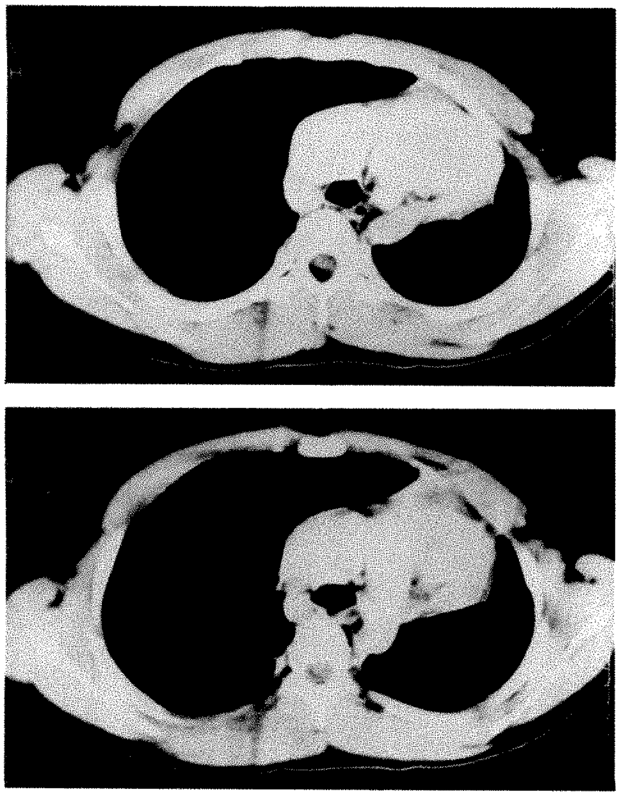

Fig 2. Chest computed tomographic scan shows a left anterior mediastinal mass and a greatly dilated superior vena cava.

Venous angiograms 3 weeks after the operation showed no stenosis. The patient was discharged on October 12, 1985.

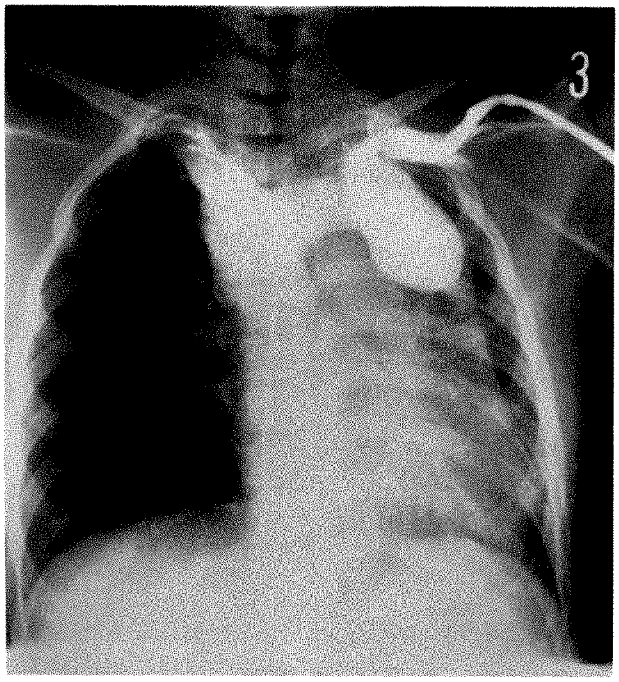

Fig 3. Venous angiogram reveals fusiform dilatation of superior vena cava and saccular dilatation of the left innominate vein.

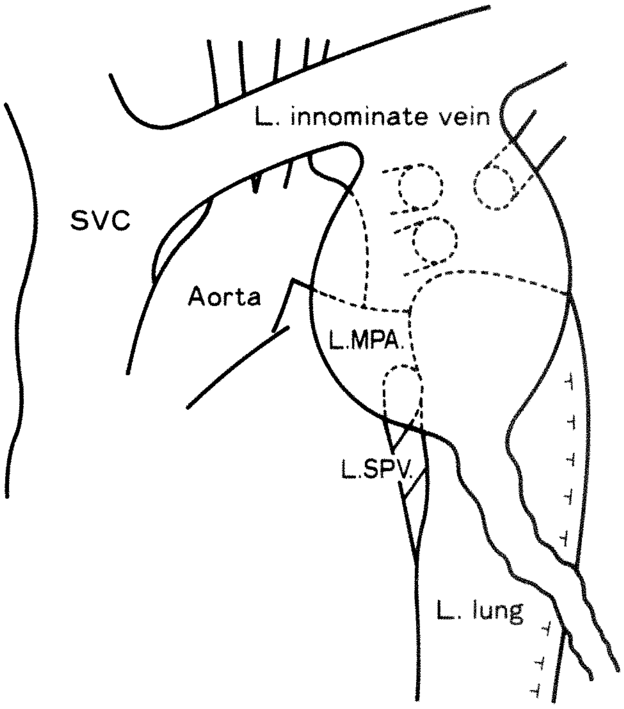

Fig 4. Anatomy of the aneurysms. (L = left; MPA = main pulmonary artery; SPV = superior pulmonary vein; SVC = superior vena cava.)

Comment

Seventeen patients with SVC aneurysm including our patient have been reported (Table 1). Until the early 1970s, exploratory thoracotomy was the main diagnostic procedure, but the introduction of superior vena caval angiography, radioisotopic angiography, and computed tomographic scans have made exploratory thoracotomy unnecessary. Furthermore, it is quite characteristic that the size and shape of superior vena caval aneurysms change with different positions and under different respiratory conditions [2, 3]. Morphologically, this disease can be divided into two subtypes: a fusiform type with partially fusiform dilatation, and a saccular type that is seen as a spherical shape with a stalk. Our patient had a fusiform superior vena caval aneurysm and a saccular aneurysm of the left innominate vein, but the diagnosis could also be an aneurysm of the left superior costal vein because three intercostal veins drained into the aneurysm as shown in Figure 4. The left lung seemed hypoplastic, and such anomaly has not been observed among other patients.

Surgical therapy other than exploratory thoracotomy was performed in 5 patients [2–5]. Abbott and colleagues [2] wrapped fragile fusiform aneurysms with polythene cellophane with good results. For three saccular aneurysms, simple surgical resection was done successfully with ligation of the stalk [3–5]. In our patient, fusiform SVC aneurysm remained untreated, and the left innominate vein aneurysm was resected. The surgical indications for this disease are controversial. However, the fusiform

Table 1. Cases of Superior Vena Cava Aneurysm

Author	Year Reported	Age (y)	Sex	Type	Treatment	Result
Abbott	1950	19	M	F	Wrapping with cellophane	Alive
Lawrence	1956	52	F	S	Resection	Alive
Gallucci	1967	28	F	S	. . .	Alive
Okay	1970	16	F	F	. . .	Alive
Bell	1970	20	M	F	. . .	Alive
Franken	1972	9	M	F	. . .	Alive
Gabriele	1972	66	M	F	. . .	Alive
Ream	1972	20	F	F	. . .	Death
Polansky	1974	11	F	F	. . .	Alive
		22	F	F	. . .	Alive
		9	F	F	. . .	Alive
Farr	1974	17	F	F	. . .	Alive
Jafari	1977	27	M	S	Resection	Alive
Heil	1978	11	M	F	. . .	Alive
Hidvegi	1979	54	F	S	Resection	Alive
Train	1981	16	M	F	. . .	Alive
Yokomise	1990	13	M	F	Resection[a]	Alive

[a] Resection of left innominate vein aneurysm.

F = fusiform; S = saccular

type seems not to need operation as 12 untreated patients with this type remained well except for 1 patient who died of pulmonary embolism probably due to infectious mononucleosis [6]. For the saccular type, surgical treatment is recommended as thrombus formation may occur.

The etiology of superior vena caval aneurysms is still unknown. Three of the four pathological specimens examined had normal venous walls, and the abnormalities in the other specimen could have been due to infectious mononucleosis. Therefore, an inherent fragility of the venous wall is not always the cause of venous saccular aneurysms. On the other hand, a 17-year-old girl who has been followed up since she was 3 years of age has been completely asymptomatic [7]. In this patient, an inherent factor seems to be important. Two patients had been injured in car accidents, but a direct traumatic cause was not clear.

The prognosis seems to be good because all of these patients, except the one who suffered from infectious mononucleosis, were alive at the time the reports were made.

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Steal Phenomenon Caused by a Parallel Branch of the Internal Mammary Artery

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We report on a patient with postoperative mammary artery steal resulting from a parallel branch of the vessel as well as from a patent first left intercostal artery, both of which had not been divided. The patient was cured of angina pectoris after embolization of both vessels.

(Ann Thorac Surg 1990;50:463–4)

Angina pectoris occurring after coronary bypass grafting using the internal mammary artery may be caused by a variety of mechanisms [1, 2]. Aside from imperfect anastomoses, rare cases of postoperative angina have been reported to result from an arterial steal phenomenon owing to intercostal and pericardial branches of the mammary artery remaining after incomplete harvesting. Also, stenosis of the left subclavian artery and congenital anomalies of the brachiocephalic vessels may contribute to inadequate coronary perfusion [3–7].

We examined a patient with a parallel branch of the left internal mammary artery and an undivided first intercostal artery branch leading to a coronary artery steal syndrome and angina pectoris after coronary bypass grafting.

A 58-year-old man underwent coronary bypass grafting for anginal pain on April 12, 1988. The left internal mammary artery was anastomosed to the occluded left anterior descending artery, and four venous connections to the right coronary and the circumflex artery systems were made. Soon after operation, moderate angina recurred. An electrocardiogram taken with the patient exercising showed clinically significant ST segment depression. A second angiography on April 6, 1989, showed a coronary artery status in accordance with the preoperative findings with all grafts patent. However, injection of contrast medium into the mammary artery orifice demonstrated a large second vessel coursing in parallel with the artery used for revascularization that obviously had not been discovered during harvest. The vessel arose from a common trunk 7 cm distal to its origin from the subclavian artery. It did not give off branches but communicated with the left epigastric artery. Furthermore, an intact first intercostal branch was opacified (Fig 1). In the late phase of the contrast medium injection, a mammary artery steal phenomena with retrograde blood flow from both mammary artery branches as well as from the left anterior descending artery occurred.

Both vessels were occluded by embolization. A special 7F catheter was directed toward the mammary artery though the left femoral artery followed by a smaller catheter inserted into the vessels to be occluded. Self-expanding coils (Tracker 18, flower coils; Target Therapeutics, San Jose, CA) of 2- and 3-mm diameter were then pushed through the catheter and placed into the parallel branch of the mammary artery and into the first branch of the intercostal artery, respectively. Both vessels occluded spontaneously during the procedure (Figs 2, 3). The patient was discharged free of anginal pain 3 days after embolization and has remained asymptomatic since then.

Comment

The use of internal mammary arteries for operative revascularization in ischemic coronary artery disease now has become a standard procedure. However, occasional poor clinical results have been attributed to inadequate flow, generally considered to result from an internal mammary artery graft of inadequate small caliber [1, 2].

In rare cases, inadequate myocardial perfusion may be caused by steal phenomena. Pelias and DelRossi [4] and Singh and associates [5, 6] reported flow diversion into undivided intercostal and pericardial branches leading to severe angina during exercise. Singh and associates found a reduction of up to 50% in the luminal diameter of the distal internal mammary artery in these patients, which was interpreted as a result of low pressure in that vessel [6, 8, 9]. In contrast, in the studies of Ivert and colleagues [10] and of Kuttler and co-workers [11], side branches of the internal mammary artery overlooked at the time of operation neither caused angina pectoris nor influenced patency.

All reported cases of angina due to a mammary artery steal syndrome after coronary revascularization were treated by interruption of the responsible vessels during reoperation with prompt disappearance of the anginal symptoms. In our patient, division of the parallel branch of the mammary artery through the left parasternal intercostal route would have been unproblematic. However, a thoracotomy would have been required to obliterate the first intercostal branch. To avoid a major operation, both vessels were therefore occluded by transarterial catheter embolization. The small self-expanding coils were easily introduced into the remaining mammary artery as well as

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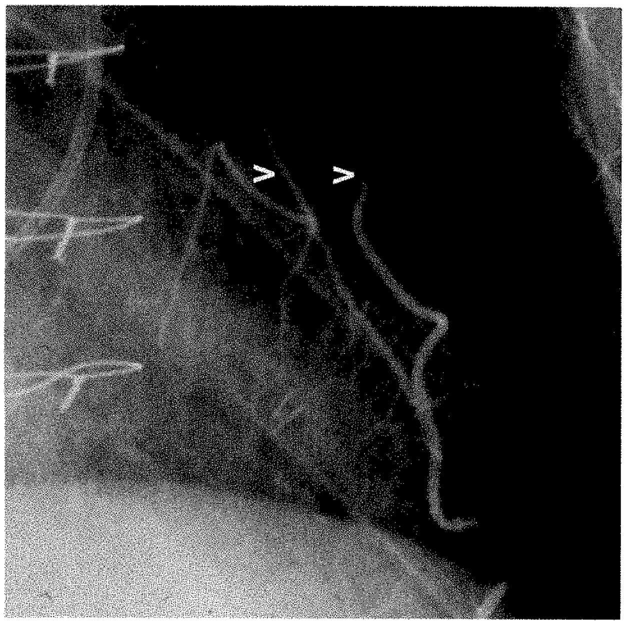

Fig 1. Angiogram taken before embolization showing the bypassed mammary artery (left) and the persisting parallel vessel (right). Three left intercostal arteries are filled through the undivided first intercostal artery.

into the first branch of the intercostal artery by a standard femoral artery approach.

This report of a parallel branch of the left internal mammary artery undivided during the harvest of its neighboring vessel emphasizes the importance of careful and meticulous harvesting of the internal mammary artery. All side branches should be divided, and the dissection should be continued to the point at which the artery appears under the subclavian vein to avoid competitive blood flow, which may spoil the result of an otherwise adequate operation. Transarterial catheter embolization has proved to be a safe and efficient method for obliteration of undivided vessels resulting in a mammary artery steal syndrome.

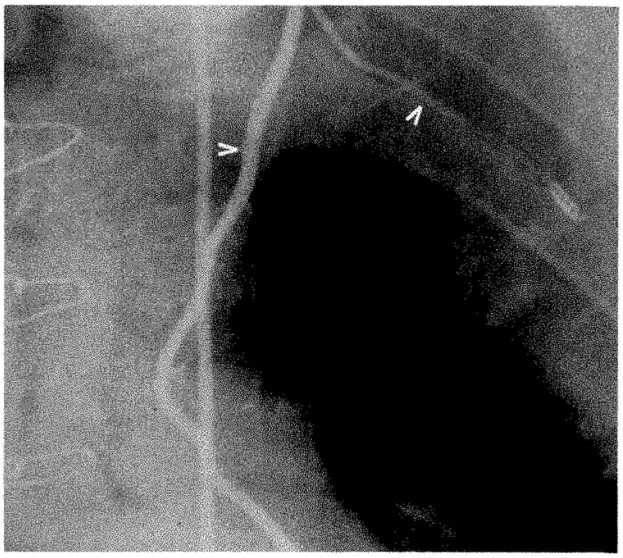

Fig 2. View after embolization showing persisting common mammary artery trunk and patent first intercostal artery, which has been embolized.

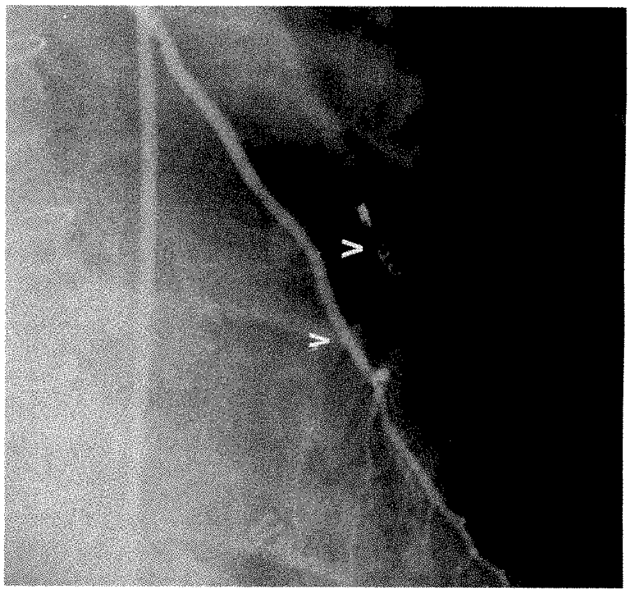

Fig 3. Angiogram taken after embolization showing the mammary artery bypass graft and the coils in the thrombosed parallel branch.

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Silastic Prosthesis Plombage for Right Postpneumonectomy Syndrome

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In rare instances, right pneumonectomy can produce progressive exertional dyspnea and reduce ventilatory reserve because of extreme mediastinal shift (right postpneumonectomy syndrome). The diagnosis can be made by bronchoscopy and computed tomography. We report a case of a 43-year-old patient in whom plombage with two Silastic breast implants produced mediastinal derotation and symptomatic relief of this syndrome.

(Ann Thorac Surg 1990;50:465–6)

In rare instances, agenesis or excision of the right lung can produce a constellation of clinical findings referred to as the right pneumonectomy or postpneumonectomy syndrome. These findings consist of rightward deviation of the mediastinum, compression of the trachea or left main bronchus by underlying vascular or osseous structures, and variable degrees of tracheomalacia. Clinically, this syndrome is characterized by progressive dyspnea (primarily on exertion), stridor, and recurrent pulmonary infections with eventual respiratory failure and death if untreated.

A 43-year-old woman underwent a right pneumonectomy on December 3, 1985, for a centrally placed 3.3-cm adenocarcinoma of her right lung. She had no evidence of metastatic disease and received no further therapy. Approximately 6 months later, paroxysmal dyspnea on exertion and stridorous breathing not associated with cough, sputum production, or hemoptysis developed. Although the patient felt that her symptoms were positional, she could not consistently describe a posture in which she felt free of dyspnea. As the frequency and severity of these episodes increased, she was taken to an emergency department several times, treated with oxygen and bronchodilators, and released. Pulmonary function testing showed moderate restriction and minimal obstruction with a considerably elevated airway resistance. Her chest roentgenogram demonstrated a shift of the trachea and mediastinum to the right hemithorax with overdistention of the left lung.

On May 14, 1987, she had a severe paroxysm of dyspnea requiring endotracheal intubation. Bronchoscopy demonstrated extrinsic compression of her left main bronchus 4 cm from the carina resulting in a luminal diameter of 3 to 4 mm. Subsequent attempts to wean her from the ventilator were unsuccessful despite bronchodilators and methylprednisolone therapy. Computed tomography on May 17, 1987, showed rightward mediastinal shift with compression of the left main bronchus over the vertebral column by the great vessels (Fig 1). There was no evidence of recurrent carcinoma.

With the premise that the extreme mediastinal shift had produced extrinsic obstruction of her left main bronchus by traction over the vertebral column and aorta, she underwent a right exploratory thoracotomy on May 21, 1987. Dense adhesions were encountered with the mediastinum adjacent to the right lateral chest wall. Mobilization of the mediastinum was accomplished, and a pericardiopexy was performed by suture fixation of the right-sided pericardium to the anterior thoracic wall. Two Silastic (Dow Corning Corp, Midland, MI) prosthetic implants (900 and 110 mL volume) were introduced into the right hemithorax to prevent any recurrent rightward mediastinal shift. Peak ventilatory pressures decreased from 26 to 21 cm H_2O during the procedure.

Postoperative bronchoscopy showed improvement of her airway diameter, and she was extubated on the second postoperative day without difficulty. A follow-up computed tomogram showed fixation of mediastinal structures in the midline with relief of left bronchial obstruction (Fig 2). She was discharged 12 days later. Follow-up spirometry showed an improvement in hyperinflation reflected by diminished forced vital capacity and forced expiratory volume at one second. A marked improvement was noted in maximum forced expiratory flow, maximum forced inspiratory flow, airway resistance, and maximal voluntary ventilation.

Comment

The right postpneumonectomy syndrome has been described as a rare complication of pneumonectomy. Adams and colleagues [1] and Szarnicki and co-workers [2] described tracheobronchial compression by this mechanism leading to respiratory insufficiency in children. Wasserman and associates [3] reported the case of a patient in whom exertional dyspnea associated with extreme rightward and posterior mediastinal shift, overdistention of the left lung, and compression of the left lower lobe bronchus over the thoracic spine developed after pneu-

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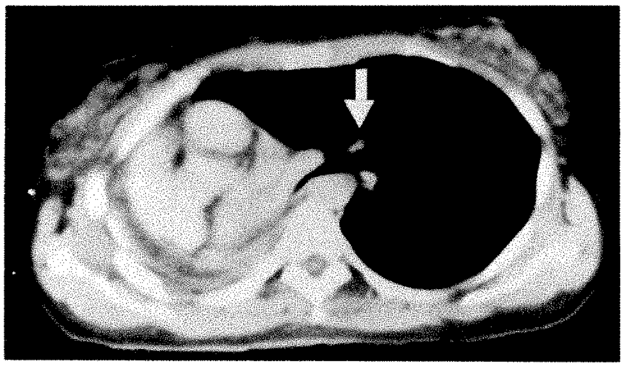

Fig 1. Preoperative computed tomogram showing compression of the left main bronchus by the aorta and vertebrae (arrow).

monectomy. Shepard and colleagues [4] later delineated the clinical and radiological signs of the right pneumonectomy syndrome as follows: (1) compression of the trachea or of the left main bronchus (demonstrable on fluoroscopy while coughing), (2) rightward mediastinal shift, (3) overdistention of the left lung, (4) counterclockwise rotation of the heart and great vessels, and (5) tracheomalacia. All 5 patients in their series were diagnosed by computed tomography, fluoroscopy, and bronchoscopy. In our patient, obstruction of the left main bronchus was demonstrated by bronchoscopy. Chest computed tomography showed bronchial compression between the pulmonary artery anteriorly and the aorta and vertebral column posteriorly.

Surgical therapy for the right pneumonectomy syndrome is directed toward correcting the tracheobronchial compression and diminishing the extreme mediastinal shift and rotation. Simple lysis of the adhesions with instillation of saline solution, plasma, and 25% albumin in 1 patient met with recurrence [3]. Pexis of the mediastinum, pericardium, or left pulmonary artery to the anterior chest wall to relieve compression led to recurrence in 2 of 6 patients [1, 3]. Division of the aortic arch with placement of a Dacron prosthesis to relieve compression of the trachea was successful in 1 patient [2]. Right phrenectomy (or crushing) has failed [3]. In 1975, Wasserman and colleagues [3] used four Silastic breast implants with good results. The same year Powell and associates [5] described the use of a Silastic breast prosthesis and several testicular prostheses in an infant. We report the successful use of two Silastic breast implants to obliterate the pneumonectomy space. These implants are available in various sizes and adapt to irregular shapes with little possibility of migration or erosion.

Progression of respiratory insufficiency after right pneumonectomy should be investigated by computed tomography to evaluate possible compression of the tracheobronchial tree by vascular structures. It can help rule out recurrent disease in pneumonectomies performed for lung cancer. Bronchoscopy can demonstrate the level of obstruction and the degree of tracheomalacia. Fluoroscopy may demonstrate tracheal or left main bronchial collapse on coughing. Spirometry and airway resistance measurements may assist in demonstrating the evolving airway obstruction caused by this syndrome. Mediastinal mobilization and pexis combined with Silastic implantation of the pneumonectomy space offers a safe and effective form of treatment.

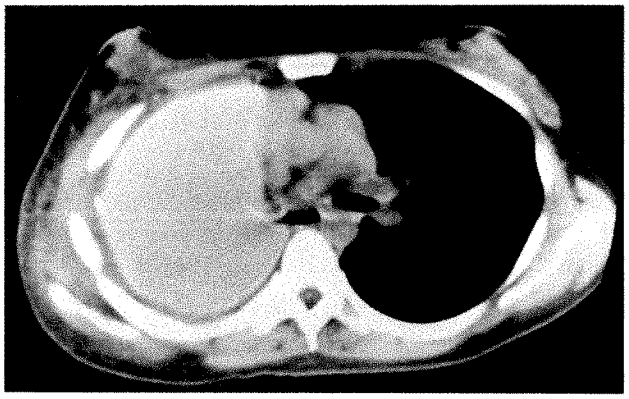

Fig 2. Postoperative computed tomogram after derotation and relief of bronchial compression. Two Silastic breast prostheses have been placed in the right pleural space.

We wish to thank Shelley Pohs for secretarial assistance.

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Tubular Supravalvar Aortic Stenosis: Replacement of Ascending Aorta in a Young Patient

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The diffuse form of supravalvar aortic stenosis represents a surgical challenge when ascending aorta and proximal aortic arch are involved. We describe a technique performed on a 14-year-old patient with normal aortic annulus and severe diffuse supravalvar aortic stenosis in which the replacement of ascending aorta and proximal aortic arch with a tubular prosthetic graft completely relieved the obstruction as confirmed by cardiac catheterization.

(Ann Thorac Surg 1990;50:467–8)

The usual surgical repair in discrete forms of supravalvar aortic stenosis consists of an aortotomy incision across the fibrous ring and insertion of a prosthetic graft across the narrowed area. Patients with the diffuse hypoplastic type of supravalvar aortic stenosis involving the ascending aorta and aortic arch require a more aggressive surgical treatment to completely relieve aortic obstruction. This report describes a new procedure for surgical correction of diffuse supravalvar aortic stenosis with normal aortic annulus.

A 14-year-old male patient, mentally retarded with "elfin-like" facies as described by Williams and co-workers [1], complained of angina pectoris on moderate exercise (walking uphill) during the last year. On examination, he had a 4/6 systolic murmur radiating to the neck vessels, and the electrocardiogram showed a severe left ventricular hypertrophy with T wave inversion in the left precordial leads. A severe narrowing of the whole ascending aorta with a normal aortic annulus and a severe left ventricular hypertrophy with a peak gradient of 240 mm Hg were demonstrated by two-dimensional echocardiography, cardiac Doppler echocardiography, and angiography (Fig 1).

Cardiopulmonary bypass was established and cardiocirculatory arrest was performed at 15°C; neck vessels and ascending aorta were clamped, and St. Thomas II crystalloid cardioplegia was administered.

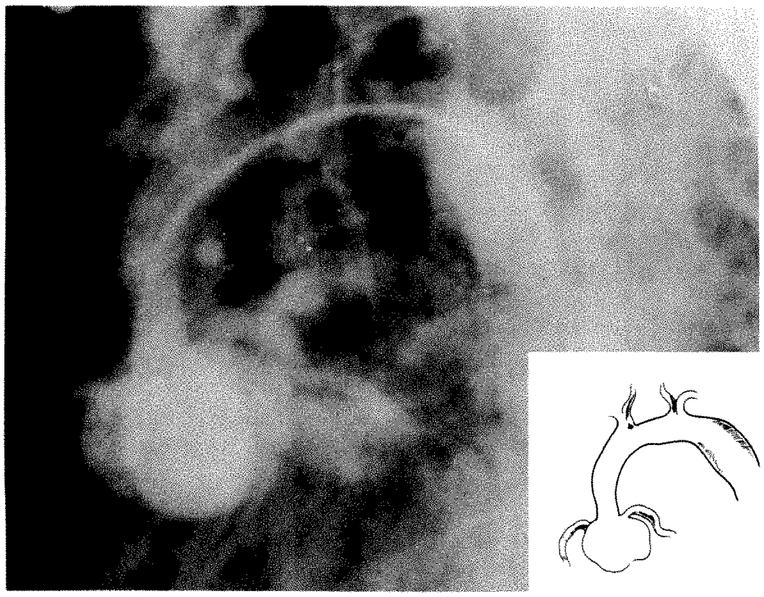

Fig 1. Preoperative angiographic demonstration of diffuse supravalvar aortic stenosis.

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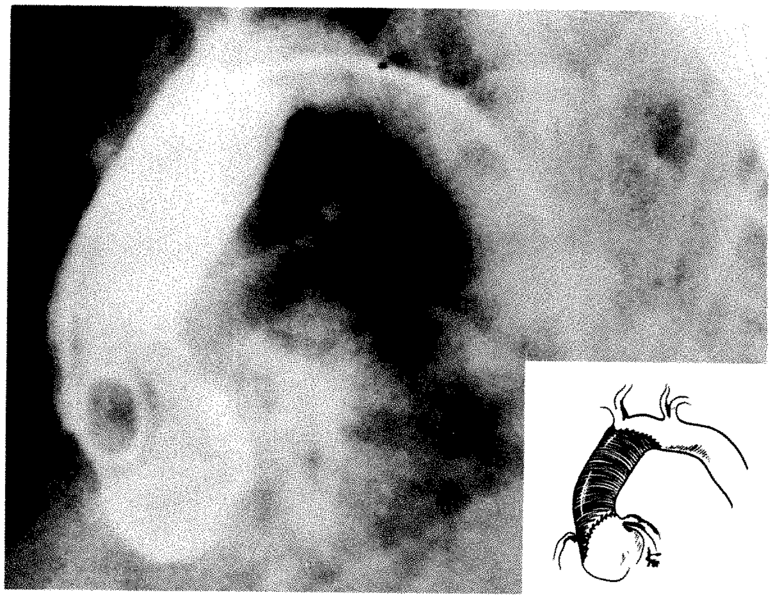

Fig 2. Postoperative angiographic demonstration of the surgical correction.

After the aortic clamp was released, a vertical aortotomy was performed across the fibrous ring, extending into the noncoronary sinus of Valsalva nearly to the aortic valve annulus.

The aortic valve cusp was asymmetric but without any stenosis, and the aortic wall was extremely thickened. Because of the severity of the lesions in the ascending aorta, we decided to replace it entirely with a 22-mm Dacron graft (De Bakey woven) that was preclotted with albumin, autoclaved, and steamed at 140°C for 5 minutes.

The distal ascending aorta just before the origin of the brachiocephalic trunk was completely cut, and the incision was prolonged across the concavity of the aortic arch to the origin of the left subclavian artery. The Dacron graft was sutured to this large opening with a continuous 5-0 Prolene suture (Ethicon, Somerville, NJ). Cardiopulmonary bypass was subsequently restarted, and the neck vessel was reperfused after the air purge. Then, with the graft clamped, proximal anastomosis was started posteriorly just above the valve commissure and the left coronary artery origin after resection of the fibrous ring. Anteriorly, the graft was cut with a long and small rounded tip and was sutured to the aortotomy that extended into the noncoronary sinus. The graft was unclamped, and the patient was rewarmed. Cardiopulmonary bypass was interrupted without any pharmacological support. No residual gradient between the left ventricle and left radial artery was detected. The patient was dismissed on the 15th postoperative day in good clinical condition and without medications (Fig 2).

Hemodynamic evaluation performed 8 months after operation showed no pressure gradient and no residual stenosis of the large ascending aorta. The patient is now asymptomatic and in good physical condition. Chest roentgenography showed a marked reduction in heart size.

Comment

The surgical relief of the discrete form of supravalvar aortic stenosis usually consists of fibrous ring resection and insertion of a gusset of prosthetic material across the narrowed area as proposed by McGoon [2], Starr [3], Doty [4], and colleagues.

In diffuse forms with severe hypoplasia of the ascending aorta, it has to be emphasized that the extreme thickness of the aortic wall makes almost virtual the lumen of the ascending aorta. Repair by conventional techniques requires the insertion of a very large patch that is difficult to design and needs long vascular sutures on pathological tissues. The early mortality is still high in these forms and midterm results are disappointing.

When an aortic annulus hypoplasia coexists with supravalvar aortic stenosis, or in very young patients, it is possible to insert a valved prosthetic conduit from the apex of the left ventricle to the thoracic descending aorta as we have done in 4 patients. Therefore, when the aortic annulus is normal, we believe that total replacement of the ascending aorta and proximal portion of aortic arch according to the technique described would be the ideal solution because it completely eliminates all the pathological tissues and the residual pressure gradients.

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Fatal Ectopic Thymoma

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We present the case of a patient who died of thymoma-induced immunological dysfunction. The neoplasm was unsuspected antemortem because of its location adjacent to the right hemidiaphragm. This appears to be the most caudad ectopic position yet encountered for a thymoma.

(Ann Thorac Surg 1990;50:469–70)

Thymoma is the most common anterior mediastinal tumor [1]. Ectopic location occurs rarely, though cervical [2], cardiac [3], and intrapulmonary [4] sites have been reported. In such cases the possibility of thymoma may not be considered until an operation or autopsy determines the diagnosis. We describe a patient with a fatal acquired immunological disorder due to an ectopic thymoma not diagnosed until autopsy.

An 82-year-old woman was seen with recurrent herpetic infections for several years and diarrhea for 1 year, and with a 25-kg weight loss. Previous extensive evaluation elsewhere had failed to identify the cause of her illness. Physical examination showed a cachectic woman with extensive mucocutaneous candidiasis but was otherwise unrevealing. Admission laboratory values included a hematocrit of 0.33 (normal, 0.36 to 0.44), white blood cell count of 10.3 × 10^9/L (10,300/μL) (normal, 4.5 to 10 × 10^9/L), total protein level of 39 g/L (3.9 g/dL) (normal, 65 to 85 g/L), and albumin level of 24 g/L (2.4 g/dL) (normal, 35 to 48 g/L). An immunoglobulin electrophoresis showed hypogammaglobulinemia with an immunoglobulin G level of 2.8 g/L (280 mg/dL) (normal, 8 to 18 g/L), an immunoglobulin A level of 0.62 g/L (62 mg/dL) (normal, 0.90 to 4.5 g/L), and an immunoglobulin M level of 0.31 g/L (31 mg/dL) (normal, 0.7 to 2.8 g/L). The patient was anergic to purified protein derivative/mumps skin testing, and the ratio of helper (T4) to suppressor (T8) lymphocytes in peripheral blood was 0.99 (normal, 2.2 ± 0.78). The chest roentgenogram on admission showed obliteration of the right cardiophrenic angle. This was initially believed to be most consistent with a pericardial cyst, but computed tomography showed a mass with soft tissue density, apparently arising from the dome of the right hemidiaphragm and adjacent to the right cardiac margin (Fig 1). The possibility that this represented normal hepatic tissue within a diaphragmatic hernia was then entertained but was eliminated by normal liver-spleen scan. Parenteral nutrition was begun, but fulminant catheter-related sepsis (*Staphylococcus aureus*) developed several days later and the patient died before further evaluation could be performed.

Autopsy showed the lesion to be a pedunculated, round, encapsulated mass. It weighed 120 g, arose from the right lower mediastinum, and measured 7.5 × 6 × 3.5 cm (Fig 2). The cut surface showed pink, fleshy parenchyma divided by thick fibrous septa. Microscopic examination of the tumor disclosed an encapsulated thymoma (Fig 3) with scant lymphoid tissue and a few abortive Hassall's corpuscles. Typical inclusions of cytomegalovirus were seen in esophageal mucosa. *Candida albicans* grew from stool, nose, and duodenum, and *S aureus* was cultured from both blood and the central intravenous catheter site. The patient was judged to have died as a consequence of immune deficiency caused by the thymoma.

Comment

Thymomas seen outside the anterior mediastinum are rare. In a review of 65 cases, Salyer and Eggleston [2] noted only one instance, which was in a cervical location. Intrathoracic metastasis from invasive thymoma is not uncommon [1], but this is unlikely to be confused with a benign thymoma as in the current example. A patient with a pedunculated thymoma arising from the lower left mediastinum has been reported by Kaplan and co-

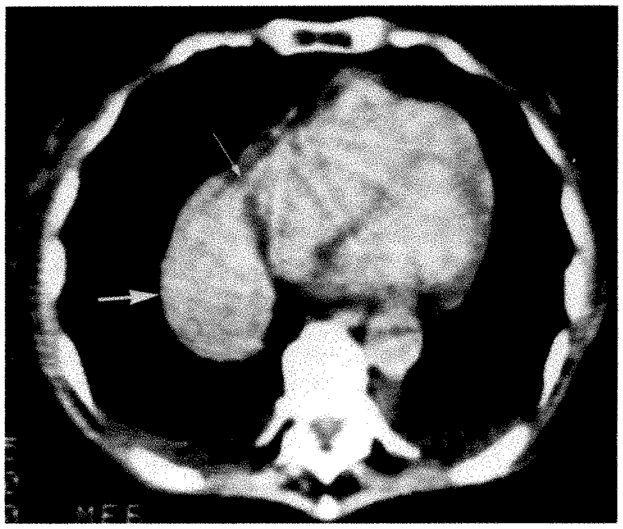

Fig 1. Computed tomographic image revealing mass (large arrow) *adjacent to heart.* Small arrow *indicates pedicle. Images immediately caudad show that the tumor abuts diaphragm.*

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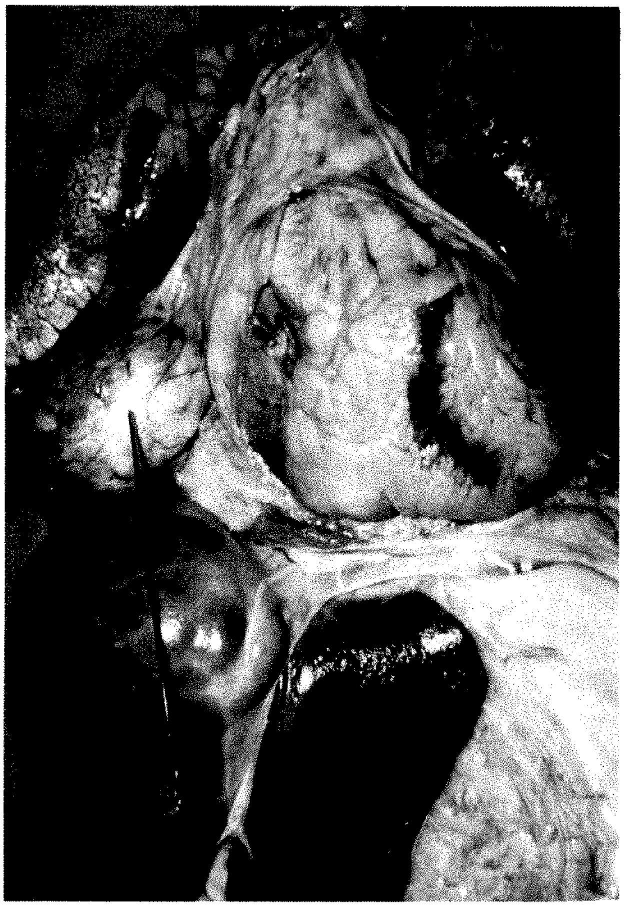

Fig 2. Autopsy view. The pointer rests on the anterior surface of the liver and its tip overlies the thymoma. The right lung is superior to the tumor and the heart is to its left.

workers [5], and Brown and colleagues [6] mentioned a nonpedunculated thymoma abutting the right heart border. In the current patient the ectopic location was so caudad that a herniated intraabdominal viscus (liver) was a working diagnosis.

Thymoma is often detected by chest roentgenography [2, 6], but computed tomography has assumed a dominant role in the evaluation of the thymus because of its excellent ability to demonstrate important anatomical relationships [6, 7]. In the patient reported by Kaplan and co-workers, computed tomography demonstrated the pedicle attached to the thymoma, aiding in the diagnosis. Gallium scan can also be valuable [5].

In our patient, the immunological dysfunction was obvious to the involved clinicians, who were also well aware of the several syndromes linking thymic disorders and T cell abnormality [1]. Although a mass was identified by chest roentgenography and computed tomography, the correct diagnosis was not considered antemortem because of the location of the tumor. Diagnostic delay was also noted in 25% of the patients in a recent Mayo Clinic series [6]. We hope that this case report, which highlights some of the difficulties encountered in making the diagnosis of ectopic thymoma, will increase awareness of this rare entity. This is important as surgical therapy can be curative. A high index of suspicion, together with appropriate imaging tests, is essential in diagnosing this potentially fatal lesion.

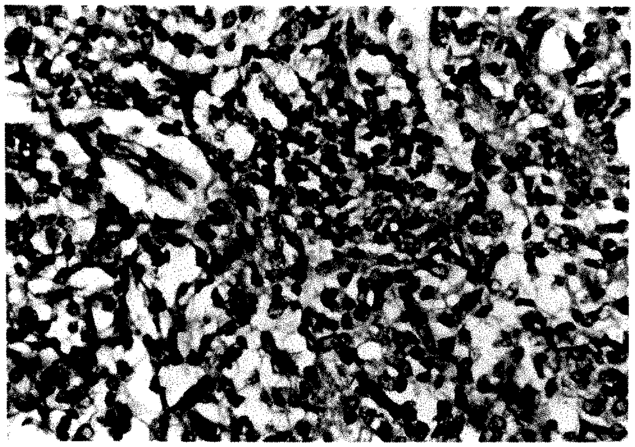

Fig 3. Photomicrograph showing neoplastic epithelial thymoma cells with pale nuclei admixed with small lymphocytes. (Hematoxylin and eosin, ×1300 before 50% reduction.)

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Intramural Ventricular Fibroma in Infancy: Survival After Partial Excision in 2 Patients

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Two infants with ventricular fibromas survived partial resection and have had satisfactory clinical results for more than 4 years. Partial excision is warranted when an unresectable tumor produces hemodynamic compromise. Long-term survival can be expected without complete resection.

(Ann Thorac Surg 1990;50:471–2)

Primary cardiac tumors in infancy and childhood are rare, with rhabdomyoma and fibroma being the two most frequently encountered. Although cardiac fibromas are characteristically benign intramural tumors, they may exhibit expansile growth resulting in obstruction, valvar dysfunction, and arrhythmia.

Early diagnosis has led to successful surgical excision in a number of cases [1–6]. Although complete excision should always be aggressively pursued, extensive growth in many patients has made complete excision impossible [7, 8].

This report details 2 infant patients with intramural ventricular fibroma in whom extensive growth precluded complete excision. Partial resection of hemodynamically obstructive tumor resulted in survival and satisfactory long-term clinical courses in both patients.

Case Reports

Patient 1

An asymptomatic 2-month-old girl with a loud systolic murmur was referred for evaluation. The infant exhibited normal growth and development. Her chest roentgenogram was normal. An electrocardiogram showed indeterminate frontal plane axis with a right ventricular conduction delay pattern. Echocardiography showed dilatation and thickening of the right ventricle with a tumor mass obstructing the right ventricular outflow tract. At cardiac catheterization, a 45-mm Hg pressure gradient across the tumor mass was identified. Cineangiography showed a nonvascular tumor mass involving the crista supraventricularis that extended along the anteromedial aspect of the right ventricular outflow tract.

Exploration performed through a median sternotomy exposed a white, firm, multilobulated tumor mass protruding anteriorly from the infundibular region involving approximately two thirds of the right ventricular free wall. This mass extended beneath the left anterior descending coronary artery and to within 1 cm of the right coronary artery (Fig 1). Because of the extensive nature of this tumor, a partial excision of the obstructing portion of the tumor mass was performed on cardiopulmonary bypass through a transverse, inferior right ventriculotomy. The pressure gradient across the obstructing tumor was reduced to 5 mm Hg after resection.

The infant recovered uneventfully and has remained asymptomatic at follow-up 3½ years later. Doppler echocardiography performed at that time showed a peak systolic flow gradient of 35 mm Hg across the right ventricular outflow tract. No substantial increase has been noted in the size of the residual tumor mass.

Patient 2

A 3-month-old infant was evaluated for a murmur. Two-dimensional echocardiography demonstrated a right ventricular outflow tract mass. Cardiac catheterization showed an elevated right ventricular pressure (45/3 mm Hg) with a 25-mm Hg peak systolic gradient across the partially obstructing tumor mass. Multiple endocardial biopsies failed to establish a histological diagnosis; however, exploratory sternotomy was performed not only to establish the diagnosis but also to evaluate the possibility of resection.

At operation, a firm, white intramural tumor mass was noted to be underlying the right coronary artery, displacing the entire pulmonary valve annulus laterally to the left. Cardiopulmonary bypass with deep hypothermia was established, and further evaluation of the extent of tumor was performed through a vertical main pulmonary arteriotomy. The tumor was noted to involve the upper portion of the interventricular septum. It was determined that the extensive nature of this tumor precluded total excision. Therefore, the obstructing portion of the tumor in the right ventricular outflow tract was resected through the pulmonary arteriotomy.

Follow-up 4 years 8 months postoperatively showed the child to be asymptomatic with normal growth and development. Doppler echocardiography was used to measure a peak systolic pressure gradient of 16 mm Hg across the

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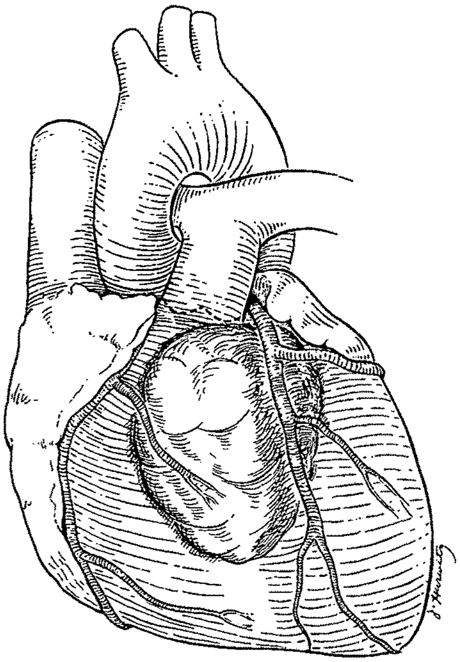

Fig 1. Tumor bulk in right ventricular outflow tract displacing the coronary vessels.

right ventricular outflow tract with no increase in tumor mass noted.

Comment

Cardiac fibromas constitute approximately 25% of the primary cardiac tumors of infancy and childhood. These pathologically benign tumors are usually solitary and intramural in location, involving the ventricular free walls, interventricular septum, or both.

Related symptoms occur frequently, with congestive heart failure being most common. Angina, syncope, and cyanosis have also been reported [1–3]. Sudden death occurred in 26% of the 31 children with cardiac fibromas collected in a review by Geha and associates [2]. Presumably, these deaths were related to tumor-induced arrhythmias, although no premorbid electrocardiograms were reported in this group.

Cardiac catheterization is used in conjunction with echocardiography to establish the diagnosis and to define the exact location and size of the tumor mass. The presence of hemodynamic compromise is also assessed.

An operation is indicated in all patients with major obstruction in whom the diagnosis is established. Complete excision should be attempted whenever feasible. Factors favoring an aggressive extirpative approach are the usual solitary nature of these benign tumors and their characteristic expansile growth, displacing rather than infiltrating the surrounding myocardium.

Extensive tumor growth may preclude safe total excision. In these cases, we advocate partial resection of the hemodynamically obstructing portion of the tumor mass. Successful partial excision of a cardiac fibroma was first reported in a 31-year-old patient by Reul and associates [8] in 1975 with a 4-year follow-up indicating the patient to be symptom-free. Two cases of incomplete resection of cardiac fibromas in children (aged 9 months and 6 years) were reported by Reece and co-workers in 1984 [6]. Both patients were reported to be asymptomatic 10 years after "debulking" procedures. These reports, combined with our present experiences, confirm that long-term survival can be achieved after satisfactory surgical palliation of cardiac fibroma. Prognosis, however, must be guarded in cases of incomplete resection because of the potential for the development of lethal cardiac arrhythmias related to continued tumor growth.

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Bronchoesophageal Fistula With an Esophageal Web

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Congenital bronchoesophageal fistulas in the adult age group are rare, with only approximately 20 cases having been recognized. All of these cases have been an isolated esophageal anomaly without other associated esophageal pathology. We present an interesting case of an adult with both symptomatic congenital bronchoesophageal fistula and proximal esophageal web.

(Ann Thorac Surg 1990;50:473–5)

A 47-year-old woman was well until 3 years before admission at Indiana University Hospital. At that time she began experiencing recurrent episodes of bronchitis. Approximately 1 year after the onset of her pulmonary symptoms, she noted dysphagia when eating solid foods and occasionally while drinking fluids. An esophagogram demonstrated a benign-appearing "weblike" stricture located in the middle third of the intrathoracic esophagus. Esophagoscopy with biopsy confirmed a mucosal-lined circumferential web 14 cm proximal to the gastroesophageal junction with normal-appearing squamous mucosa throughout the remainder of the intrathoracic esophagus. The patient underwent a series of esophageal dilations with symptomatic improvement. Six months before admission, however, she again noted frequent episodes of bronchitis, along with intermittent coughing spells, most notable after drinking liquids. Repeat esophagogram demonstrated a bronchoesophageal fistula (BEF) between the mid-esophagus and the bronchus intermedius (Fig 1). The esophageal web appeared to be restenosed and was located just proximal to the esophageal origin of the fistula. Physical examination was remarkable only for a moderately obese woman who had frequent episodes of coughing during examination, as well as coarse rhonchi and expiratory wheezing auscultated in the right lower lung.

Intraoperative bronchoscopy demonstrated a pinpoint fistula orifice in the posterior membranous wall of the bronchus intermedius. The patient then underwent a right thoracotomy through the fifth intercostal space. At the level of the sixth thoracic vertebra a BEF was identified. The fistula was well circumscribed, of uniform diameter, and noninflamed; it was easily separated from the surrounding lung parenchyma by a layer of loose areolar tissue. The entire fistula, from the mid-esophagus to the distal bronchus intermedius, was circumferentially dissected (Fig 2A). The fistula was stapled near the bronchial orifice and transected at the level of the esophagus. The proximal esophageal web was exposed by extending the esophagotomy approximately 2 cm cephalad (Fig 2B). The web was circumferentially excised. The esophageal mucosa was reapproximated and the esophagotomy was closed. Histological evaluation of the fistula revealed a tubular structure 8 mm in diameter with a nonkeratinized, stratified squamous epithelium and an adventitial layer (Fig 3A). The remainder of the wall was composed of fibrous tissue with disorganized bundles of smooth muscle and nervous tissue (Fig 3B). The patient had an uneventful recovery including a normal esophagogram on the 7th postoperative day. She remains completely asymptomatic 16 months postoperatively.

Comment

Congenital BEF first seen in adulthood is extremely rare, with approximately two dozen reported cases in the

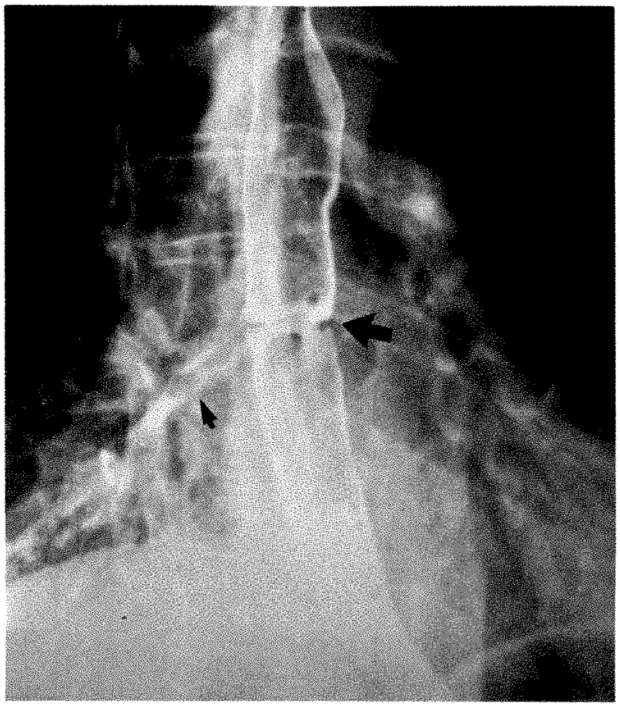

Fig 1. Esophagogram demonstrating web (large arrow) *and bronchoesophageal fistula* (small arrow).

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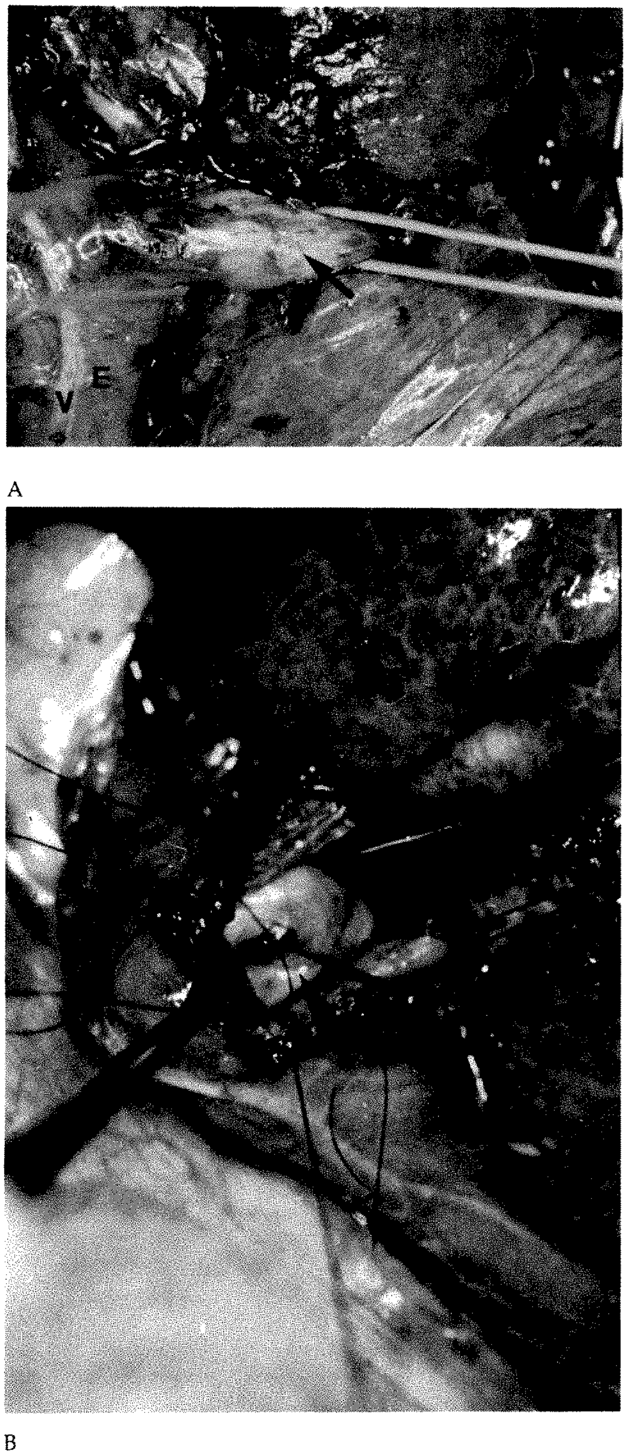

Fig 2. (A) Bronchoesophageal fistula (arrow) *to the bronchus intermedius after dissection (E = esophagus; V = vagus). (B) Esophageal web* (arrow) *found cephalad to the esophagotomy after excision of the bronchoesophageal fistula.*

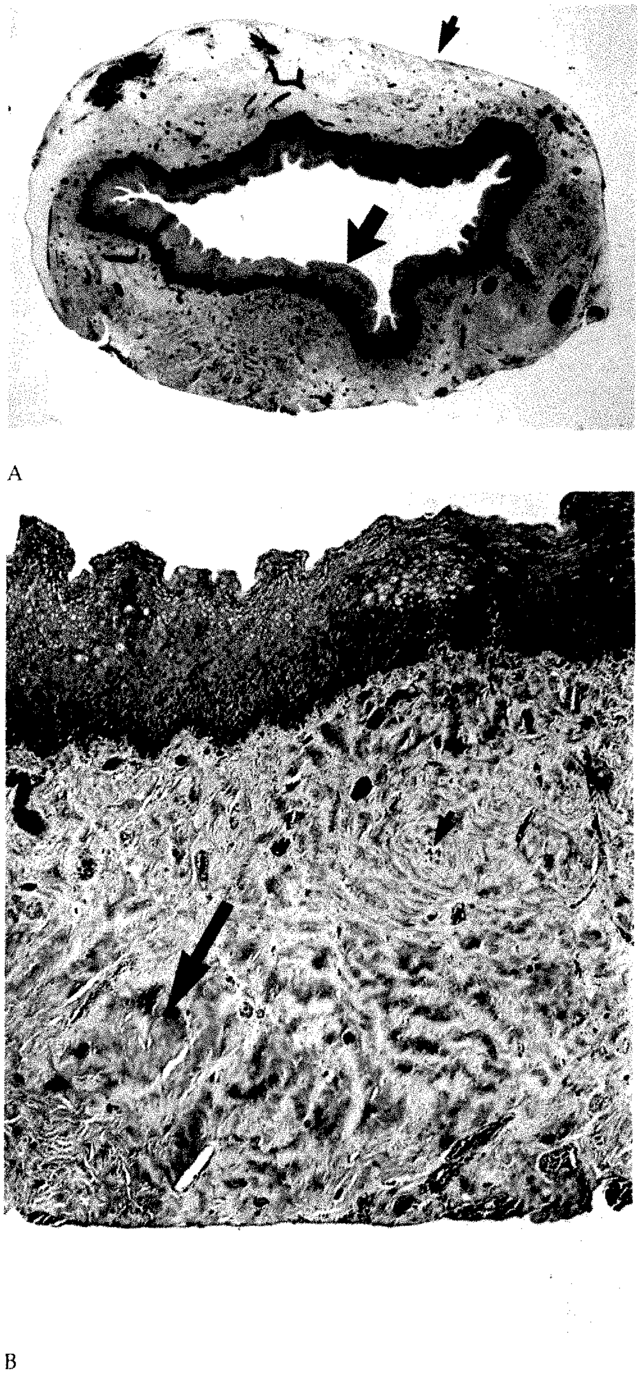

Fig 3. (A) Cross-section photomicrograph of bronchoesophageal fistula demonstrating a well-differentiated, nonkeratinized, stratified squamous epithelium (large arrow) *and an adventitial layer* (small arrow). *(Hematoxylin and eosin, ×10.) (B) High-power photomicrograph of fistula wall identifying fibrous tissue with disorganized bundles of smooth muscle* (large arrow) *and nervous tissue* (small arrow). *(Hematoxylin and eosin, ×51.2 before 3% reduction.)*

literature [1–3]. Most commonly these fistulas have connections into a lobar or segmental bronchus; however, they occasionally communicate with sequestrated lung segment [4–7]. Various conditions have been proposed to explain the oftentimes late presentation including a cephalad or nondependent relationship of the airway ostium to the esophageal ostium (N-shape), the presence of a thin mucosal membrane over the esophageal ostium that may act as a one-way valve, and compression of the fistula by peristalsis preventing drainage into the bronchus [1, 3, 7, 8].

Histologically, congenital BEFs have a well-organized, stratified squamous or bronchial epithelium, identifiable muscularis mucosa or smooth muscle within the wall, and absence of major surrounding inflammation [1, 2, 6, 8]. Lack of inflammation about the fistula is a typical finding which greatly facilitates dissection [7].

Our patient's clinical situation was unusual in that previously reported adult BEFs have occurred as an isolated esophageal anomaly. The presence of a proximal esophageal web associated with a rostrally directed BEF and a competent lower esophageal sphincter may account for this patient's late presentation. Gross and histological findings of the web and adjacent esophagus showed no evidence of inflammation or characteristics suggestive of peptic stricture. It is doubtful that reflux was related to the cause of the esophageal web in this case because of the absence of either symptomatology or pathological findings, normal-appearing squamous mucosa of the intrathoracic esophagus, and the relatively high intrathoracic location. We believe the BEF was congenital in nature for several reasons. First, although the pulmonary symptoms were seemingly exacerbated by esophageal dilation, bronchitis of the right lower lobe was seen 1 year before the onset of dysphagia. Additionally, the fistula was well defined and easily dissected from the surrounding lung parenchyma. Finally, histological examination was consistent with a congenital origin.

Congenital fistulas between the esophagus and tracheobronchial tree result from developmental abnormalities in the fetal foregut secondary to incomplete division of these structures during the first trimester in utero. In the pediatric age group, tracheoesophageal fistula is most commonly associated with proximal esophageal atresia. Although preoperative esophageal manometry to detect any motor dysfunction was not done, the proximal esophageal web in this patient may represent a forme fruste of esophageal atresia in the spectrum of congenital esophageal fistulas to the tracheobronchial tree seen in the adult age group [9, 10].

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Successful Surgical Treatment of Incessant Automatic Atrial Tachycardia With Atrial Aneurysm

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A 9-year-old boy with heart failure and long-term incessant atrial tachycardia mimicking dilated cardiomyopathy was treated surgically. Intraoperatively he was found to have atrial aneurysm, and the ectopic automatic focus was located at the base of it. Excision of the aneurysm including the focus without using cardiopulmonary bypass cured the tachycardia and heart failure.

(Ann Thorac Surg 1990;50:476–8)

Incessant focal atrial tachycardia is a rare arrhythmia and causes cardiac failure mimicking dilated cardiomyopathy [1–3]. This report describes a case of preoperatively diagnosed incessant atrial tachycardia with ectopic automatic focus, which was associated with right atrial aneurysm.

A 9-year-old boy who had been suffering from incessant tachycardia was admitted to our hospital with symptoms of palpitation and dyspnea. He was referred with a diagnosis of dilated cardiomyopathy with long-standing supraventricular tachycardia and cardiomegaly. On admission he was orthopneic with a respiratory rate of 28/min, heart rate of 130/min, and blood pressure of 90/70 mm Hg. Physical examination showed hepatomegaly, peripheral edema, and a gallop rhythm with a grade 2/6 holosystolic murmur at the apex on heart auscultation. Chest roentgenogram revealed pulmonary congestion, bilateral pleural effusion, and marked cardiomegaly with a cardiothoracic ratio of 0.72. Electrocardiogram on admission showed supraventricular tachycardia with a rate of 100 to 200 beats/min, which was essentially the same as the one seen when he was 9 months old (Figs 1a, b). Echocardiography exhibited no structural abnormality except for markedly reduced left ventricular contractility with fractional shortening of 0.15. Catheterization of the heart disclosed no intracardiac shunt or obstruction. Left ventriculography confirmed an extremely dilated ventricle

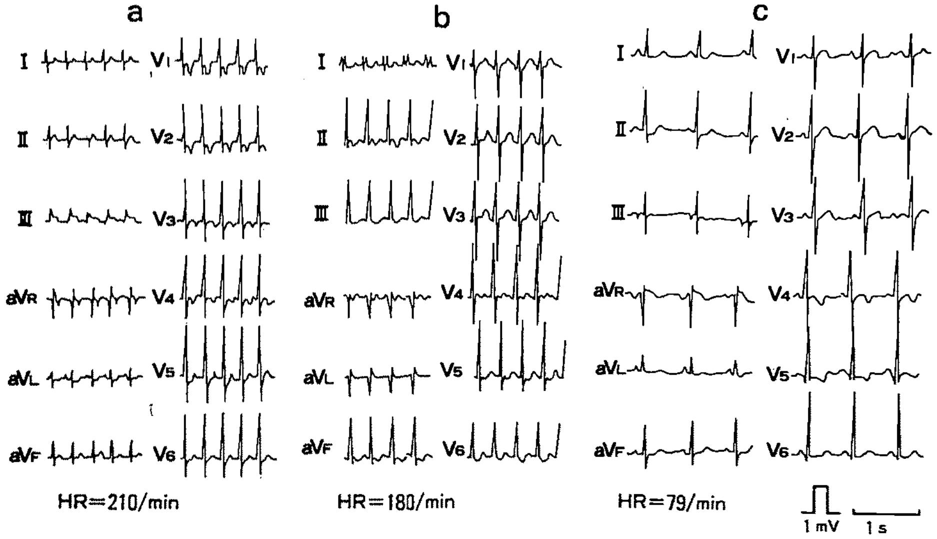

Fig. 1. Electrocardiogram (a) at 9 months of age, (b) on admission, and (c) after operation. (HR = *heart rate.)*

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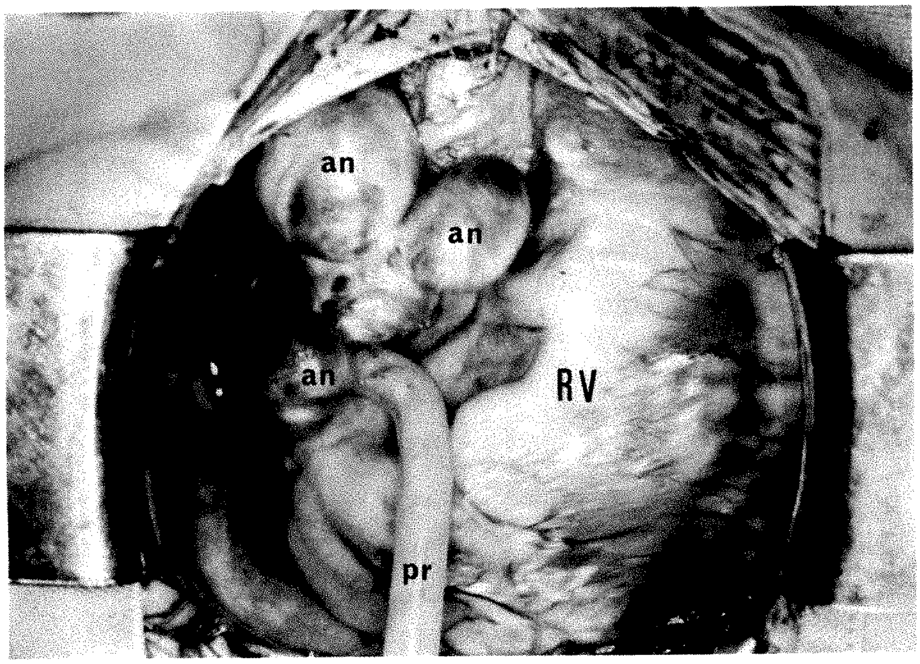

Fig. 2. Intraoperative view of right atrial aneurysm. Note the three saccular aneurysms. (an = *aneurysm;* pr = *probe used for mapping;* RV = *right ventricle.)*

and poor contractility with an end-diastolic volume index of 205 mL/m^2 and ejection fraction of 0.16.

At electrophysiological study for the evaluation of supraventricular tachycardia, rapid atrial pacing at a rate faster than his own atrial rhythm captured the atrium, but on the termination of pacing, the tachycardia immediately resumed without the intervention of sinus rhythm, and it had a "warm-up" phenomenon with a cycle length of 490-430-380-350 ms. Therefore the tachycardia was diagnosed to be automatic. By endocardial mapping, the earliest activation site was located at the anterior wall of the right atrium. After the electrophysiological study, it was concluded that the underlying disease of this patient was not cardiomyopathy but incessant automatic atrial tachycardia. To eliminate the tachycardia, surgical excision of the ectopic automatic focus was indicated.

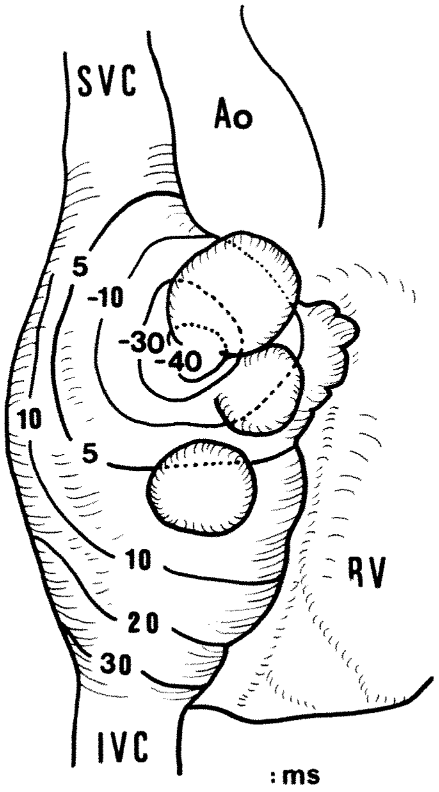

Fig. 3. Intraoperative epicardial mapping. The earliest activation site is at the base of the largest aneurysm. (Ao = *aorta;* IVC = *inferior vena cava;* RV = *right ventricle;* SVC = *superior vena cava.)*

When the pericardium was opened, aneurysm formation was found on the right atrium between the anterior wall and the appendage (Fig 2). There were three aneurysms, and the largest one was 3.2 cm in diameter. Epicardial mapping localized the focus of the tachycardia at the base of the largest aneurysm (Fig 3). Excision of aneurysms together with the focus was done without cardiopulmonary bypass. The tachycardia ceased immediately and sinus rhythm emerged (Fig 1c). This was the first time that the sinus rhythm had ever been recorded in this patient.

Histological examination revealed that the wall of the aneurysm was composed of one or two strands of cardiac muscle with epicardial fibrosis and endocardial fibroelastosis. A group of small cells was found at the site of the earliest atrial activity. It resembled a structure of sinus node, and was considered the ectopic automatic focus.

The patient had an uneventful postoperative course with normal sinus rhythm and was discharged from the hospital in a good condition. Left ventricular contractility improved gradually after the operation, and at the nineteenth postoperative month, the left ventricular ejection fraction was 0.62 and the fractional shortening was 0.33

by echocardiography. Cardiomegaly disappeared and the cardiothoracic ratio dropped to 0.48. The patient has been asymptomatic without any medication.

Comment

There are some reported cases of atrial aneurysm associated with atrial tachycardia [4, 5], but the mechanism has not been fully evaluated yet. Olsson and associates [1] reported a case of incessant ectopic atrial tachycardia with right atrial aneurysm that was very similar to our case, but in that case it was not confirmed whether the tachycardia was due to automaticity or reentry circuit. The tachycardia in our patient could not be terminated by overdrive atrial pacing. The overdrive pacing captured the atrium, but on termination of pacing, the tachycardia resumed immediately without intervention of sinus rhythm, and the electrocardiogram showed "warm-up" phenomenon. The earliest activation site was localized at the anterior wall of the right atrium by endocardial mapping. Hence the tachycardia was diagnosed as ectopic automatic atrial tachycardia.

The histological structure of the earliest activation site showed a resemblance to sinus node. The aneurysm in our patient was a true aneurysm, and the causal correlation between the aneurysm and the small cells at the focus is unclear. The clinical presentation of the reported cases of Varghese and co-workers [5] and Olsson and associates [1] have a number of similarities to the present case: (1) multiple true atrial aneurysms, (2) incessant ectopic atrial tachycardia, (3) no intracardiac abnormality, and (4) tachycardia since near birth that was congenital. Therefore, the combination of these clinical pictures may constitute a new syndrome. As heart failure can be cured by cessation of tachycardia [6], children with poor cardiac function mimicking cardiomyopathy should be carefully examined, and an electrophysiological study is essential for accurate diagnosis.

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Surgical Repair of Type II Truncus Arteriosus Without a Conduit

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A technique for reconstructing the right ventricular outflow tract in an infant with type II truncus arteriosus without using a prosthetic conduit is described. The truncal root is transected, and the confluence of branch pulmonary arteries is brought anterior to the aorta by using Lecompte's maneuver. The aorta is then reconstructed directly with an end-to-end anastomosis. The right ventricular outflow tract is reconstructed by anastomosing the posterior wall of the confluence directly to the apex of the vertical right ventriculotomy. A glutaraldehyde-preserved pericardial patch is then placed anteriorly to complete reconstruction of the right ventricular outflow tract.

(Ann Thorac Surg 1990;50:479–81)

The operative procedure for truncus arteriosus has changed little since McGoon and associates [1] first described homograft-valved conduit repair in 1967. The surgical treatment of truncus arteriosus in infants still poses a serious challenge. Some surgeons have reported improved results of definitive repair in infants with the use of prosthetic valved conduits [2] and valveless conduits [3]. However, all conduits are prone to becoming stenotic and to promoting endocarditis; in addition, valve failure is a problem in valved conduits [4]. When these complications occur, reoperation to replace the conduit is necessary. Even though a second operation is successful in a majority of patients, they are at an increased risk of mortality and morbidity. Moreover, the possibility of recurring complications and the need for subsequent reoperations still exist [5].

The success of Lecompte's [6] maneuver in reconstructing the pulmonary outflow tract during the arterial switch procedure prompted us to use a similar technique to reconstruct the right ventricular outflow tract in a 16-day-old infant who had type II truncus arteriosus, high pulmonary blood flow, and low pulmonary vascular resistance. A report of this operation is described herein.

Case History

A 7-day-old female infant weighing 3.8 kg who had tachypnea, failure to thrive, signs of congestive heart failure, left-to-right shunting, and pulmonary vascular overload was examined. Echocardiography confirmed the diagnosis of truncus arteriosus. Cardiac catheterization, which was performed when the infant was 9 days of age, revealed truncus arteriosus (Collett and Edwards, type II) with a nonrestrictive ventricular septal defect and an aortic oxygen saturation of 91%. Because of persistent high pulmonary flow, low pulmonary vascular resistance, and continued heart failure, early operation was recommended and undertaken when the child was 16 days of age.

Technique

The patient is placed on cardiopulmonary bypass using bicaval cannulation: one cannula is inserted through the right atrial wall, and a 10F aortic cannula is placed high on the ascending aorta or transverse arch. The patient is cooled to 24°C, during which time both pulmonary arteries are extensively mobilized as previously described [7]. The pulmonary arteries are temporarily clamped at their origin to avoid pulmonary overperfusion during cooling, and the ductus or ligamentum arteriosum is divided. The ascending aorta is then clamped, cardioplegic solution is injected, and bypass flow is reduced to 30 to 60 $mL \cdot kg^{-1} \cdot min^{-1}$. The truncal root is then transected so that the pulmonary confluence is separated from the aorta (Fig 1A) and brought anterior to the aorta using Lecompte's [6] maneuver (Fig 1B). The aorta is reconstructed with a direct end-to-end anastomosis using continuous monofilament suture [7]. A high vertical right ventriculotomy is made, and the supracristal ventricular septal defect is closed with a Dacron patch (Meadox Medicals, Oakland, NJ) extending to the apex of the ventriculotomy. The right ventricular outflow tract is then reconstructed by anastomosing the posterior wall of the pulmonary confluence to the apex of the right ventriculotomy. A dome-shaped hood of autogenous glutaraldehyde-preserved pericardium is created to connect the remainder of the pulmonary confluence to the ventriculotomy incision, thus forming a nonobstructive pathway for right heart output (Fig 1C). The patient is warmed at high flow rates and then weaned from cardiopulmonary bypass. Postoperative management is based primarily on monitored left atrial pressure.

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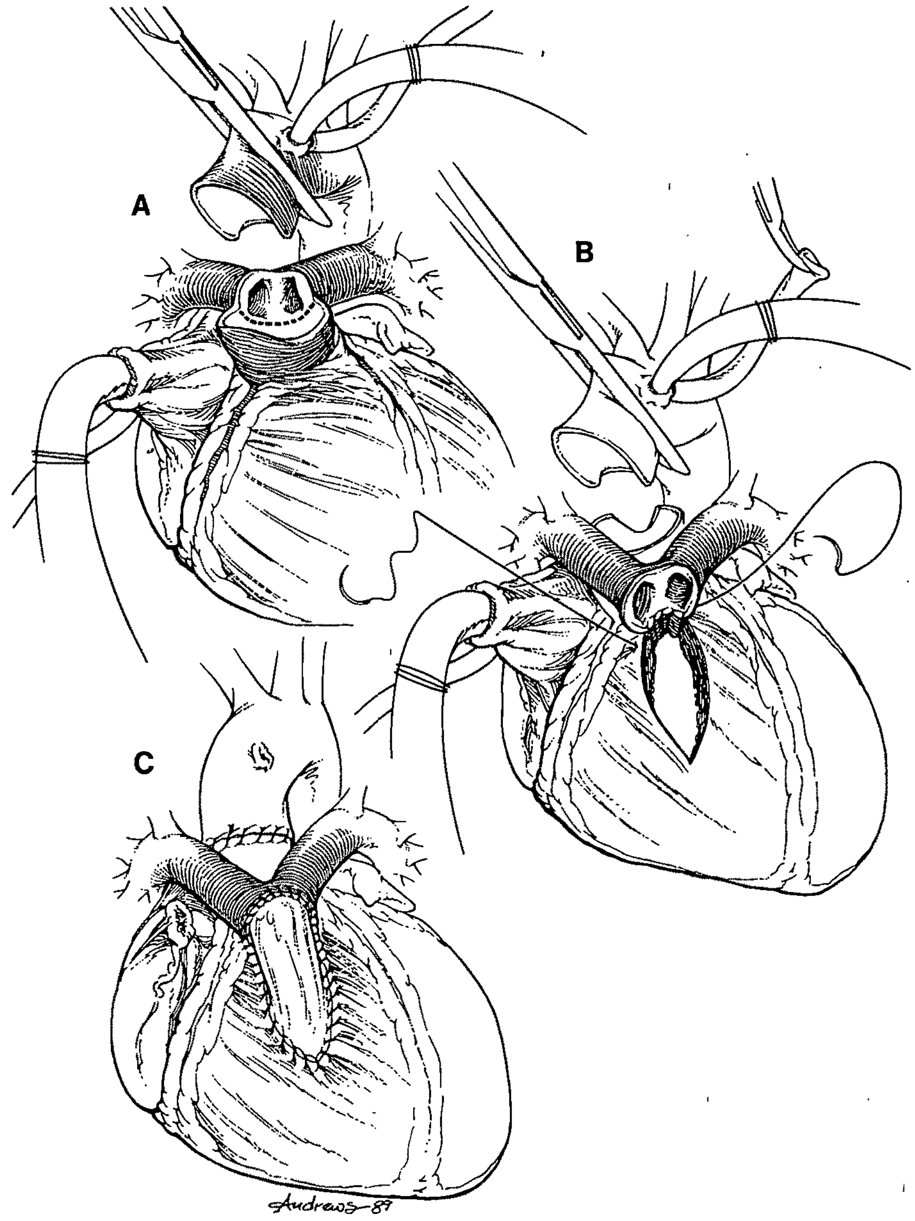

Fig 1. Surgical technique for repair of truncus arteriosus (see text).

Comment

We have used a modified Lecompte technique to repair a type II truncus arteriosus. The method does not require the use of a prosthetic conduit or valve and, thus, may help prevent some of the early and late complications associated with their use [2, 3, 7]. Besides reducing the risk of infectious complications, the technique may also reduce, or at least delay, the need for further operations, since the pulmonary outflow reconstruction should enlarge as the child grows.

Our patient, a 16-day-old infant weighing 3.8 kg, had high pulmonary blood flow and low pulmonary vascular resistance. After operation, she required inotropic support and treatment for congestive heart failure. The patient was discharged from the hospital 34 days from the date of operation, and at the time she was taking only digoxin. An echocardiogram obtained postoperatively showed pulmonary regurgitation with a small left to right shunt at the ventricular level. Most patients in whom a transannular patch has been used experience such pulmonary regurgitation, but this can be well tolerated for many years, and their response to exercise remains adequate if there is no clinically significant residual obstruction [8].

Lecompte [6], Weldon (in a discussion following the article by Ebert and co-workers [2]), Reid [9], and their associates have described similar techniques for reconstructing the right ventricular outflow tract by anastomosing the pulmonary artery directly to the right ventricle. All patients in Lecompte's series had monocusp valves inserted during the procedure, but 2 patients died of pulmonary regurgitation despite this fact. Lecompte and associates believe that continued investigation of different valves and better insertion methods is necessary. We did not use a valve in our patient, who has had no adverse effects. Likewise, the patient of Reid and associates [9] did not have a valve inserted, but their technique is for instances in which the pulmonary confluence arises from the left lateral margin of the aortic root. The method described herein can be used when the pulmonary confluence arises posteriorly.

The advantages afforded by this technique may make it suitable for use in most cases of truncus arteriosus requiring operation in infancy. Evaluation of early results in a larger series of patients will be required to determine operative mortality, since the effect of an absent competent pulmonary valve on early mortality is as yet undetermined. Finally, long-term follow-up of a series of patients who have undergone surgical repair with this method will be necessary to make a firm comparison of its effectiveness with that of the previously described techniques.

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Diuresis in Hemodynamically Compromised Patients: Continuous Furosemide Infusion

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We have used continuous infusion of furosemide to achieve diuresis in patients who are stable but hemodynamically compromised after heart operations. With a loading dose of 20 mg and a continuous infusion of 4 to 10 mg of furosemide per hour, mean 24-hour urine output was 5.7 L (238 ± 65 mL/h). Potassium replacement was 115 ± 20 mmol [115 ± 20 mEq/L]. Cardiac index, central venous pressure, and diastolic pulmonary artery pressure did not change significantly, even though hemodynamic support was decreased in each patient. Continuous furosemide infusion is a simple, effective, and reliable method to achieve diuresis in select patients.

(Ann Thorac Surg 1990;50:482–4)

Patients who are hemodynamically compromised after heart operations are usually markedly edematous, but diuresis can be difficult to achieve because of the need to maintain adequate cardiac preload. Copeland and associates [1] first reported that continuous intravenous infusion of furosemide provided gentle, sustained diuresis in hemodynamically stable patients after elective cardiac operations. We have applied this technique to hemodynamically compromised patients, and have achieved substantial diuresis with no adverse hemodynamic effects. In this report, we review our initial experience with this technique.

Material and Methods

Patients

Data were collected on 6 patients who received continuous furosemide infusion. Three patients had coronary artery bypass grafting, 2 had mitral valve replacement, and 1 had orthotopic heart transplantation. All of the patients had a satisfactory cardiac output (cardiac index greater than 2.2 L · min^{-1} · m^{-2}) and good renal function (creatinine level less than 140 μmol/L [1.6 mg/dL]), but all were receiving inotropic support and 4 had an intraaortic balloon pump in place (Table 1). All were fluid overloaded by at least 6 L from the preoperative state, as judged by intake and output since the day of operation. All patients survived and were discharged from the hospital.

Technique

The solution is made by adding 100 mg of furosemide to 100 mL of 5% dextrose. A loading dose of 20 mg of furosemide is given intravenously, and the infusion is started at 4 to 6 mg per hour. The infusion can be increased if more diuresis is needed, but we generally do

Table 1. Patient Characteristics and Hemodynamic Support Before and After Furosemide Infusion

Patient No.	Age (y)	Operation	IABP		Inotrope	Dose of Inotrope	
			Pre	Post		Pre	Post
1	70	Emergency CABG	1:1	1:2	Dobutamine (μg · kg^{-1} · min^{-1})	11	5
					Epinephrine (μg/min)	7	5
2	66	MVR	None		Dobutamine (μg · kg^{-1} · min^{-1})	5	0
3	73	CABG	1:1	1:2	Dobutamine (μg · kg^{-1} · min^{-1})	7	5
					Epinephrine (μg/min)	2	2
4	38	Heart transplant	None		Isoproterenol (μg/min)	6	3
5	63	CABG	1:1	1:2	Dopamine (μg · kg^{-1} · min^{-1})	3	3
6	58	Emergency redo MVR	1:1	Out	Dobutamine (μg · kg^{-1} · min^{-1})	3	3
					Dopamine (μg · kg^{-1} · min^{-1})	2	2

CABG = coronary artery bypass grafting; MVR = mitral valve replacement; post = after furosemide infusion; pre = before furosemide infusion.

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Table 2. Hemodynamic and Laboratory Data Before and After Furosemide Infusion

Time	CI ($L \cdot min^{-1} \cdot m^{-2}$)	CVP (mm Hg)	PAD (mm Hg)	Na (mmol/L)	K (mmol/L)	BUN (mmol/L)	Cr (μmol/L)
Pre	2.82 ± 0.2	15.5 ± 4.3	17.0 ± 4.3	136 ± 4.0	4.4 ± 0.6	7.1 ± 3.4	80 ± 30
Post	2.80 ± 0.5	12.3 ± 1.7	16.0 ± 4.1	133 ± 3.1	3.8 ± 0.3	6.4 ± 2.4	100 ± 50

BUN = serum blood urea nitrogen; CI = cardiac index; Cr = serum creatinine; CVP = central venous pressure; K = serum potassium; Na = serum sodium; PAD = pulmonary artery diastolic pressure.

not exceed 10 mg per hour. Urine output is followed hourly. Serum potassium level is measured every 4 hours and replaced as necessary. Electrolytes, blood urea nitrogen, and creatinine level are checked every 12 hours. The infusion is generally stopped after 24 hours. No additional measures are necessary and the remainder of the patient care is according to standard protocols.

Results

The data are reported as mean value ± standard deviation. Preinfusion and postinfusion hemodynamic and laboratory data are presented in Table 2. The range of furosemide infusion was 4 to 10 mg per hour with a mean of 4.8 mg per hour. All patients had moderate and sustained diuresis with a mean 24-hour urine output of 5.7 L (238 ± 65 mL/h). The actual potassium losses in the urine were not measured, but the mean potassium replacement in a 24-hour period that was necessary to keep the serum potassium level greater than 3.5 mmol/L [3.5 mEq/L] was 115 ± 20 mmol [115 ± 20 mEq]. Cardiac index, central venous pressure, and pulmonary artery diastolic pressure remained relatively constant during the infusion (Figs 1–3). Inotropic drugs or intraaortic balloon pumping were able to be decreased or discontinued in all patients during the infusion (see Table 1).

Comment

Lawson and colleagues [2] reported that diuresis could be achieved in patients with refractory edema by continuous intravenous infusion of furosemide. Copeland and associates [1] subsequently found that continuous infusion of furosemide provided sustained diuresis in patients with good hemodynamic function after a cardiac operation. We have modified this technique by combining a loading dose with a continuous infusion, and by applying the technique to patients who are stable but hemodynamically compromised.

There are several advantages to this technique. First, substantial diuresis can be achieved without adverse hemodynamic effects, even in patients who require inotropic support or intraaortic balloon pumping. Second, the effects of the furosemide infusion can be easily regulated. Hourly urine output can be increased or decreased by adjusting the infusion rate, and diuresis stops within a few hours after the infusion is discontinued. Finally, the solution is simple to prepare, requires no special monitor-

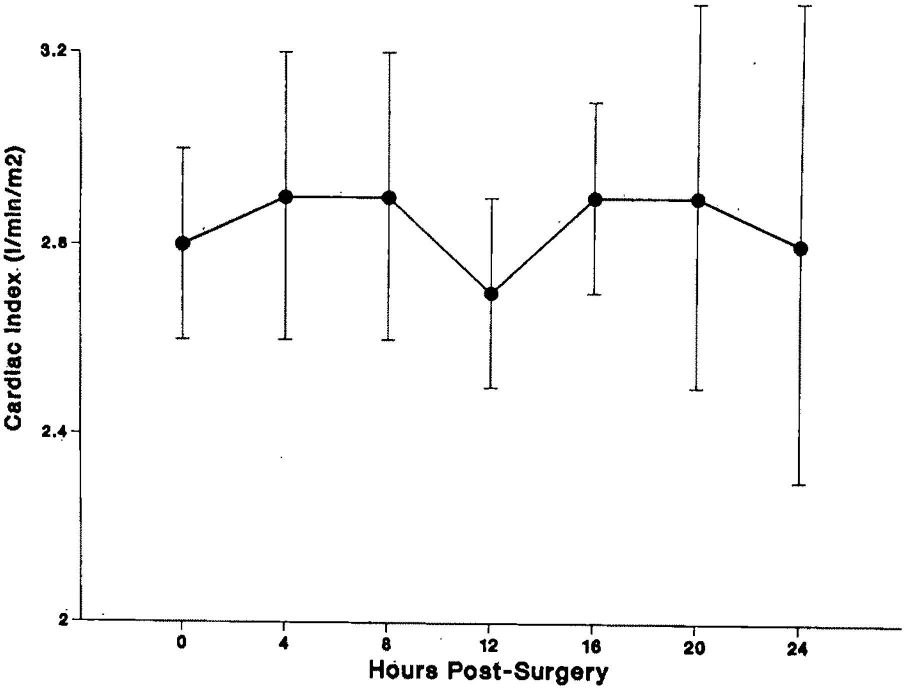

Fig 1. Cardiac index was satisfactory and stable throughout the period of furosemide infusion.

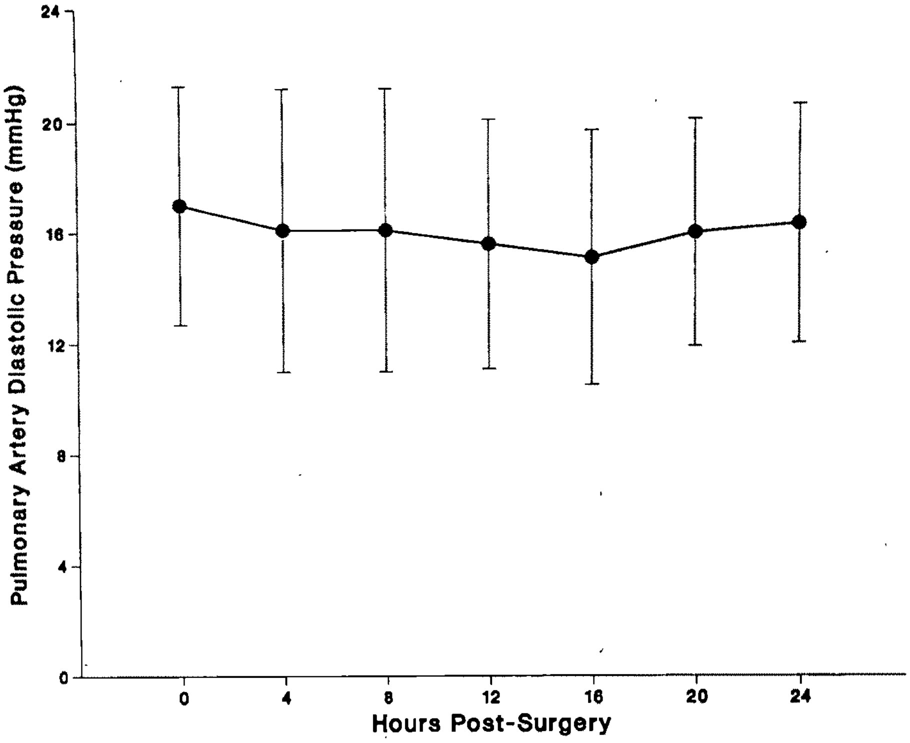

Fig 2. Pulmonary artery diastolic pressure remained nearly constant during the infusion.

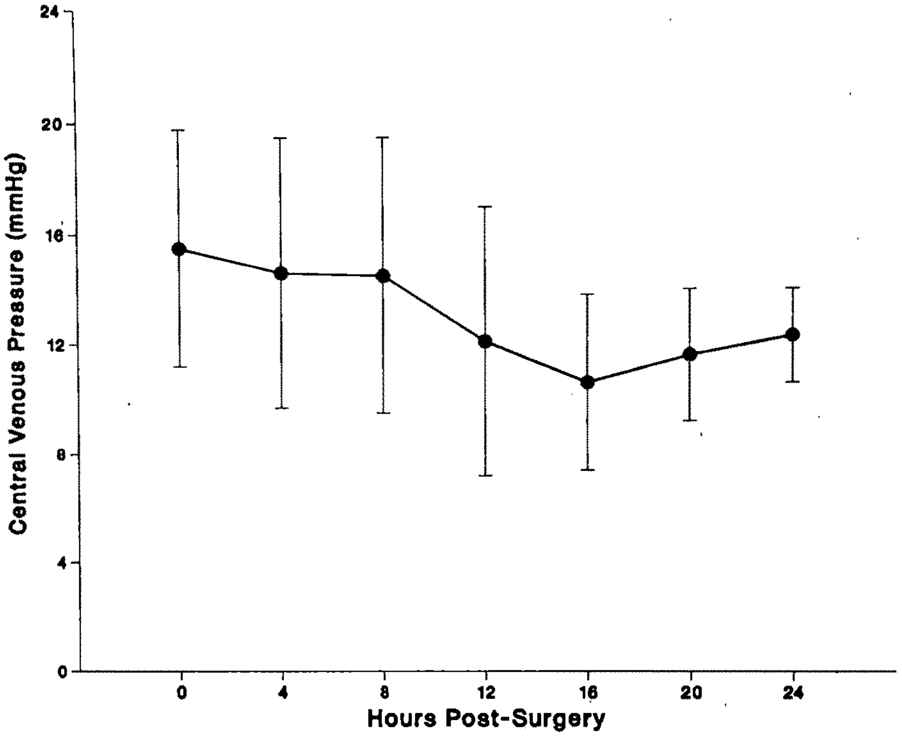

Fig 3. Central venous pressure decreased slightly during the infusion, but the change was not statistically significant.

ing or facilities, and can be administered through a peripheral intravenous line. We have not induced renal dysfunction or seen otologic toxicity, but these problems might occur if the infusion is continued for greater than 24 hours. Potassium replacement is necessary, but the amounts are not excessive. We have found continuous infusion of furosemide to be a simple, reliable, and effective method for achieving diuresis in select patients.

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Platysma Musculocutaneous Flap for Reconstruction of Trachea in Esophageal Cancer

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In 2 patients with advanced cervical esophageal cancer invading the trachea, total laryngoesophagectomy with resection of the posterior portion of the trachea and lymph node dissection of the bilateral neck and superior mediastinum was carried out. The partial defect in the trachea was repaired with a platysma musculocutaneous flap. A permanent tracheostoma, composed of the tracheal remnant anteriorly and the platysma musculocutaneous flap posteriorly, was made just over the manubrium sterni.

(Ann Thorac Surg 1990;50:485–7)

Cervical esophageal cancer widely invading the trachea is not usually radically operated on because of the difficulty of reconstructing the trachea. We tried a new reconstructive procedure using a platysma musculocutaneous flap after removing the membranous wall of the trachea. We performed the procedure in 2 patients, and satisfactory results were obtained. This report describes 1 case history and details of the procedure.

Case History

A 70-year-old man complained of pharyngeal pain and dysphagia for 4 months. Radiologic examination of the upper gastrointestinal tract revealed a spiral-type filling defect of the cervical esophagus, measuring approximately 4.5 cm in length and extending from 1.0 cm below the pharynx to the upper margin of the manubrium sterni. Esophageal endoscopy revealed an ulcerative lesion of the esophagus, and biopsy of the lesion showed squamous cell carcinoma. Bronchoscopy revealed multiple erosions with diffuse redness on the membranous portion of the trachea. The tracheal lesion extended from 4 to 8.5 cm below the vocal cords and was strongly suggestive of direct invasion by the esophageal tumor. Right recurrent nerve paralysis was noted. Computed tomographic scan also suggested direct invasion of the trachea.

Total esophagectomy with combined resection of the larynx and posterior portion of the trachea and dissection of the bilateral cervical and superior mediastinal lymph nodes was carried out. The esophagus was reconstructed with the transverse colon through the posterior mediastinal route, and the trachea was reconstructed as described in the next section.

Technique

A U-shaped skin incision reaching to 6 cm below the upper margin of the manubrium sterni was made (Fig 1). An extended platysma musculocutaneous flap attached to the fascia of the pectoralis major muscle was raised and a midline skin incision of about 7 cm was added for easy exposure of the upper half of the sternum. The sternum was sawed at the midline from its upper margin to the third intercostal space and cut transversely at this level making an inverted T shape. Then the superior anterior mediastinum was opened. After lymph node dissection of the bilateral paraesophageal, paratracheal, middle, and inferior internal jugular chains, the cervical esophagus was isolated with the larynx and upper part of the trachea and transected at the level of the hypopharynx. About 8 cm of the posterior portion of the trachea that was invaded by cancer was removed with the tumor, and the tracheal cartilage was preserved (Fig 2). The intrathoracic esophagus was bluntly removed through the median sternotomy without thoracotomy.

After confirming the surgical margin of the trachea to be free of cancer cells by intraoperative pathological examination, we reconstructed the defect in the trachea. The extended platysma musculocutaneous flap was deepithelized, leaving the portion corresponding to the tracheal defect (see Fig 1). Then the flap was inserted into the superior mediastinum, and the epithelial portion was sutured to the tracheal margin, thus constructing the posterior wall. A tracheostoma was made above the sternum (Figs 3, 4). The skin defect created by the musculocutaneous flap was covered with a free skin graft from the right groin.

We performed this procedure in 2 patients. In both patients, the postoperative course was uneventful. Major complications such as bleeding, leakage, and infection did not occur. Respiration could be easily controlled through the intratracheal cannula.

At 1 year 4 months and 1 year of follow-up, both patients are alive without recurrence of the cancer.

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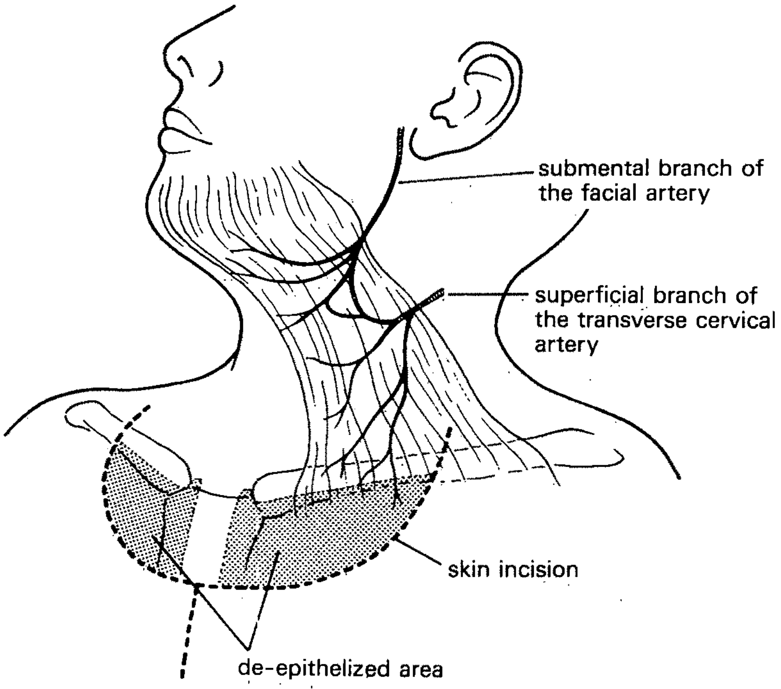
submental branch of the facial artery
superficial branch of the transverse cervical artery
skin incision
de-epithelized area

Fig 1. A U-shaped skin incision for obtaining the platysma musculocutaneous flap. Shaded area *indicates deepithelized portion.*

Comment

Many attempts have been made by surgeons to cure cervical esophageal cancer invading the trachea, focusing on the management of the involved trachea. Grillo's [1] tracheostomy at the anterior mediastinum is well known as a procedure to be used after wide resection of the trachea. Orringer and Sloan [2] reviewed the experience with 17 patients in whom anterior mediastinal tracheostomy was used, and the results are excellent, but 1

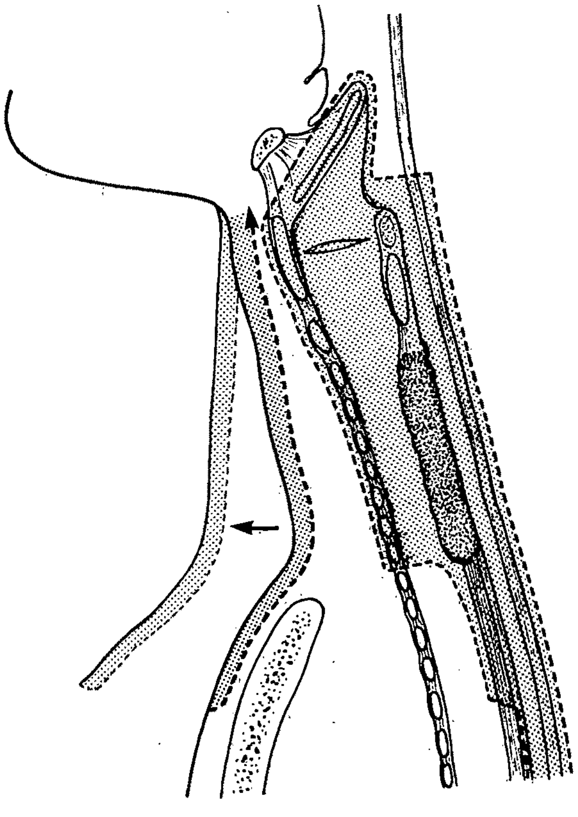

Fig 2. Shading *indicates area of extended resection.* Arrow *shows the cutting line to make a platysma musculocutaneous flap.*

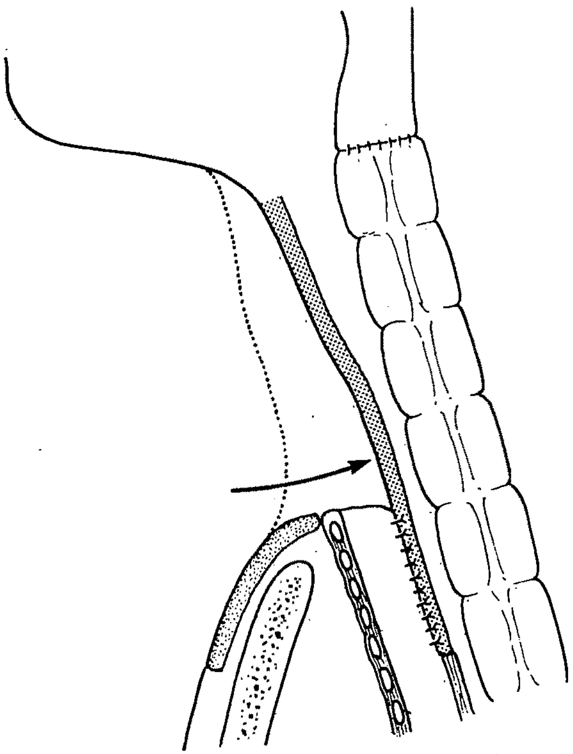

Fig 3. Transposition of the platysma musculocutaneous flap to the posterior defect in the trachea. The defect created by the flap is covered with a skin graft.

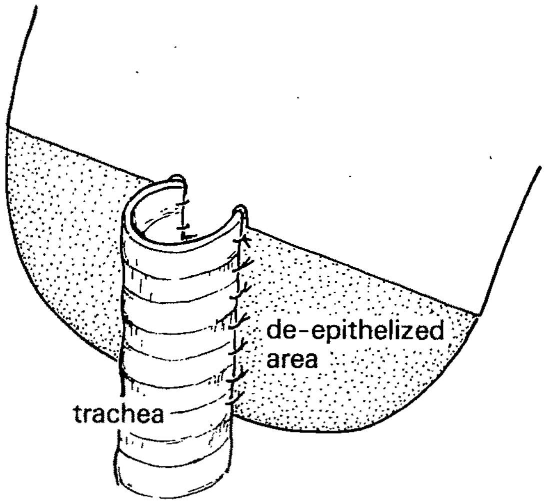

Fig 4. Schema of the procedure of covering the tracheal defect with the flap.

patient died of innominate artery rupture. In 1985, Krespi and co-workers [3] improved Grillo's procedure by using a new technique to protect great vessels with a pectoralis musculocutaneous flap. With this procedure, the risk of major complications after mediastinal tracheostomy such as suture line breakdown, infection, and bleeding could be avoided. Ong and colleagues [4] reported a procedure to close a small defect in the posterior wall of the trachea with a deltopectoral flap in a patient with locally advanced esophageal carcinoma.

Our procedure was done in 2 patients with cervical esophageal carcinoma extensively invading the posterior portion of the trachea. One of advantages of this procedure is to be able to make the tracheostoma in the cervical region by a simplified technique. We did not experience any fatal complications such as innominate artery rupture or infection. Our procedure must be safe, because the great vessels are covered by their own chest wall.

As the platysma is supplied with blood from two vascular pedicles, the submental branch of the facial artery and the superficial branch of the transverse cervical artery [5], the submental branch of the facial artery is preserved when making the flap in our procedure.

The disadvantage of this procedure is that dyspnea sometimes develops months after operation unless an intratracheal cuffless silicone cannula is used. However, both of the present patients no longer need the intratracheal cannula all day long.

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Infant ECMO Cannulation Technique Allowing Preservation of Carotid and Jugular Vessels

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A technique is presented for cannulation of the cervical vessels for extracorporeal membrane oxygenation. Reconstruction of the vessels can be accomplished after decannulation. Doppler ultrasound confirms patency after decannulation in most cases.

(Ann Thorac Surg 1990;50:488–9)

Venoarterial extracorporeal membrane oxygenation (ECMO) has been shown to be effective therapy for various types of severe respiratory failure, especially in the newborn [1–4]. The right carotid and jugular vessels are the best cannulation sites for infant ECMO [1, 3, 4]. The most widely used cannulation technique employs permanent ligation of the jugular vein and carotid artery cephalic to the cannulation sites [3, 4]. Although it is believed to be a safe technique, the short-term complications of carotid/jugular ligation may be difficult to separate from neurological problems resulting from intracranial bleeding, cerebral edema, and other factors during ECMO [3, 4]. The long-term effects are largely unknown, as no survivor of infant ECMO has been followed into the adult years. We therefore prefer to preserve these vessels when possible and have used the cannulation technique described herein for newborns as well as older children.

Technique

With the patient supine on a shoulder roll with the head rotated to the left, the carotid and jugular vessels are exposed through a short longitudinal incision at the lower anterior sternomastoid border. Fine Prolene (Ethicon, Somerville, NJ) oval pursestring sutures are placed in each vessel and threaded through short Silastic (Dow Corning, Midland, MI) tourniquets. Each vessel is encircled twice with Silastic vessel loops (Neomedix Systems, Sydney, Australia). After heparinization, cannulas are inserted through a longitudinal incision using a sidebiting clamp. Air is then removed from the cannulas and they are connected to the ECMO circuit. The Silastic vessel loops are tied securely around the cannulas and vessels and the knots are secured with medium clips (Fig 1). The pursestring sutures are then secured in their tourniquets with a few additional clips. The wound is closed in layers with the cannulas exiting from the upper pole, tied to the tourniquets. An antibiotic-soaked dressing is applied over a cutaneous wound closure.

When ECMO support is no longer required, the wound is reopened, the vessel tapes and pursestrings are removed, and the vein and artery are allowed to bleed anterogradely and retrogradely to ensure that no thrombus is present. The vein and artery are then repaired with fine Prolene sutures. The arteriotomy may be closed transversely to avoid stenosis.

Comment

The vessel-loop technique provides immediate and excellent hemostasis around the cannulas during ECMO and, being minimally traumatic, allows reconstruction at the time of decannulation. Carotid and jugular flow during

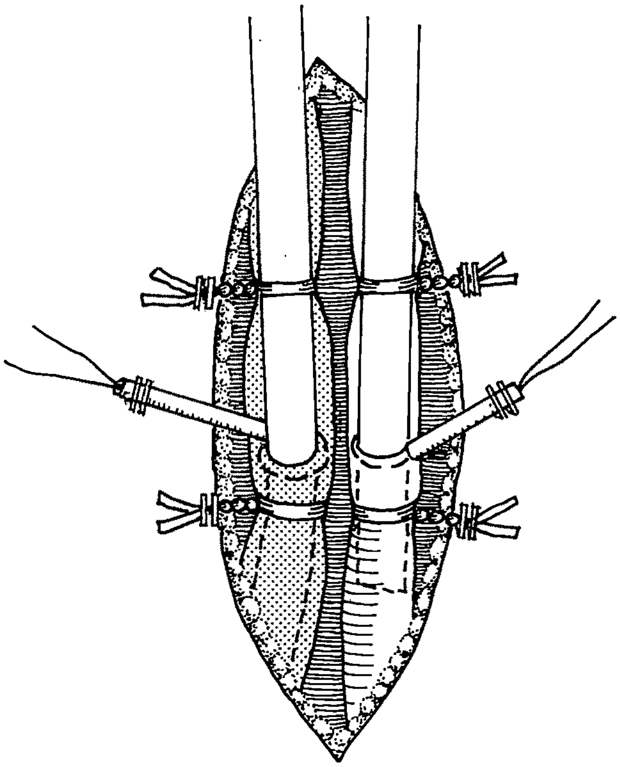

Fig 1. The cervical vessels are cannulated through a narrow pursestring suture and secured with Silastic vessel loops and tourniquets. At decannulation the vessel incisions are closed primarily.

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ECMO are interrupted with this technique, but in small infants the cannulas themselves normally occlude the vessels. The vessel loops do not add to this problem. In patients with larger vessels in which the cannulas were not occlusive we have sometimes omitted the vessel loop snares, although this technique has been less satisfactory from the point of view of hemostasis.

Ten ECMO survivors (6 with vessel loops and 4 without) had reconstruction of the cervical vessels at the time of decannulation. The age range was newborn to 13 years (median, 3 days); weight, 2.7 to 55 kg (median, 3.8 kg); and time on ECMO, 39 to 265 hours (mean, 117 hours). In 1 patient (aged 20 months) a mild left hemiplegia developed, and another patient (aged 13 years) had a diffuse encephalopathy that resolved over 1 month. No other neurological problems were identified. Doppler ultrasound studies performed 1 to 13 months afterward revealed normal carotid flow in all patients, although 1 had minor turbulence without a detectable pressure gradient (vessel-loop technique). Jugular vein flow was normal in 7 patients. In 1 newborn the vein could not be imaged adequately, and in 2 patients (non–vessel-loop technique, ages newborn and 20 months) the jugular vein was occluded, with collateral flow detectable.

Although the long-term neurological outlook may or may not differ in patients having reconstruction rather than permanent ligation, we believe that the latter procedure is usually unnecessary. Carotid and jugular continuity can be reestablished in the majority of cases using this technique.

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HISTORICAL VIGNETTE

A Practical Mechanical Respirator, 1929: The "Iron Lung"

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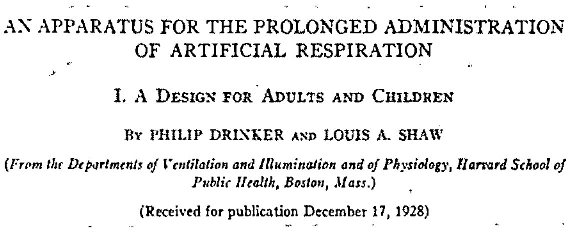
No satisfactory mechanical respirator existed before 1929, when Philip Drinker and Louis Shaw described an apparatus of their own design. This machine was in the form of a cylindrical tank enclosing the patient's body and chest, leaving the head outside the chamber under atmospheric pressure. Air pumps, later a bellows, raised and lowered pressure within the tank to assume the entire work of breathing. Popularly named the iron lung, the Drinker respirator supported thousands of patients afflicted with respiratory paralysis during the polio era. It was being superseded by positive-pressure airway ventilators just as the polio era came to a close. Today the Drinker respirator has disappeared virtually without a trace. Although its disadvantage was its cumbersome size, we must concede that it supported patients over the long term with fewer complications than do the respirators of today.

(Ann Thorac Surg 1990;50:490–3)



AN APPARATUS FOR THE PROLONGED ADMINISTRATION
OF ARTIFICIAL RESPIRATION

I. A DESIGN FOR ADULTS AND CHILDREN

BY PHILIP DRINKER AND LOUIS A. SHAW

(From the Departments of Ventilation and Illumination and of Physiology, Harvard School of Public Health, Boston, Mass.)

(Received for publication December 17, 1928)

Fig 1. Title page of the 1929 paper by Drinker and Shaw. (Reproduced from the Journal of Clinical Investigation, *1929;7:229–47, by copyright permission of the American Society for Clinical Investigation.)*

Those thoracic surgeons who began surgical training before 1954 or 1955 remember well the standard mechanical respirator of that time, a horizontal steel cylinder almost a meter in diameter, 2 meters in length, standing on metal legs but movable on casters. A large bellows located underneath the cylinder, driven by an electric motor, made continuous sighing and wheezing noises. Only the patient's head protruded from the cylinder. Air-sealing portals on each side, however, could admit the nurse's or physician's arms for access to the patient inside. Patients dependent on the respirator could be brought outside it only during provision of alternative means of respiratory support such as continuous bag-breathing by an anesthesiologist. A combined hand lever and foot pedal enabled one person to continue to work the bellows in case of electrical failure. This cumbersome mechanical monster, known familiarly as the iron lung, was for a quarter of a century the only reliable machine of its kind and for all its shortcomings, a lifeline for thousands of patients afflicted with respiratory failure caused by poliomyelitis.

The general outline of the iron lung can be foreseen in Sauerbruch's illustrations of 1904, showing his primitive Unterdruck chamber for thoracic surgery [1, 2]. The head of the patient or experimental animal protruded outside the chamber, with a more or less airtight seal at the neck, while chest and body remained inside the chamber under the effects of negative atmospheric pressure. All that was missing from Sauerbruch's chamber was cyclic alternating pressure, but that essential detail was not to be added for another 25 years.

A New Therapeutic Possibility

No reliable method for prolonged respiratory support, or artificial respiration as it was then called, existed when Philip Drinker and Louis Shaw reviewed the subject in 1929 (Fig 1) [3]. Their listing of discarded techniques ranged from the "Schäfer method" of external chest compression, widely taught in the schools, through external bellows and the "Pulmotor," to chambers of various kinds, and finally to the cuirass pattern respirator recently patented in 1928 by Eisenmenger of Vienna. The latter, designed as a chamber partially enclosing the chest on its anterior surface, was insufficiently effective for just this reason. Drinker and Shaw described an apparatus of their own design, a cylindrical metal chamber large enough to accommodate the patient's entire body without restriction (Fig 2). One end of the cylinder could be released and would slide out on casters together with the stretcher on which the patient's body lay (Fig 3). Airtight closure of the chamber could be accomplished quickly by securing levers around the rim. A series of rubber collars of different sizes were fabricated to provide an essentially airtight seal at the patient's neck. The large bellows used in later models were not part of the original design; instead, two high-speed electric blowers alternately exhausted air from the tank and blew it back in. One blower was a spare and could be shut down or removed for servicing while the

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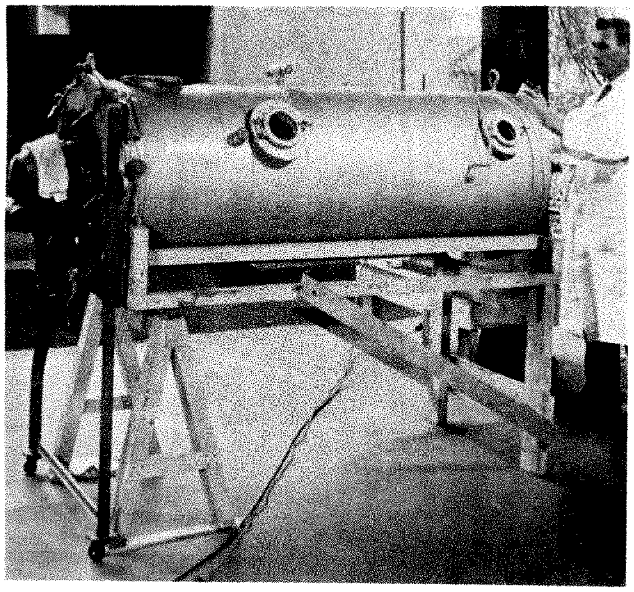

Fig 2. Original cylindrical tank respirator with a "patient" inside. (Reproduced from the Journal of Clinical Investigation, *1929;7: 229–47, by copyright permission of the American Society for Clinical Investigation.)*

other continued to run. "Their noise," said the authors, "is a drawback in hospital work. We expect shortly to substitute pumps of more silent operation" [3].

After demonstrating that it was impossible to ventilate a patient by the Schäfer method sufficiently to render him or her apneic, Drinker and Shaw showed that this could be accomplished easily with their apparatus. Threshold pressures that induced breathing against the subject's will were found to be between ±5 and ±10 cm H_2O in normal subjects. The air blowers could develop positive and negative pressures within the chamber with as high as ±60 cm H_2O at rates of 10 to 40 cycles/min. To avoid the problems of severe respiratory alkalosis, intermittent oral spirometry was recommended so that the machine could be "regulated to conform with the average respiratory volume per minute per kilogram of body weight for the particular individual." This being an entirely empirical value, nomograms for minute volume of ventilation were subsequently developed through study of large numbers of patients in respirators [4], but many potential corrections were necessary, the most important being for the presence of fever or infection.

A cooling apparatus was controlled by thermostats within the tank. Drainage tubes, intravenous lines, and the like could pass into or out of the chamber through small holes or pipe taps. Patients in respiratory failure after thoracotomy could be managed with this apparatus; the chest drainage tube was brought out of the chamber through a sealing porthole to connect with the water-seal bottle and suction apparatus on the floor outside.

Prophetically, the first patient treated with the Drinker respirator in 1929 was an 8-year-old child with respiratory paralysis from poliomyelitis. Despite respiratory support for 122 hours, the child died of bronchopneumonia and congestive failure. "During the time the child was in the respirator, she was able to talk, sleep, and take nourishment while the pumps were running. . . This case and another described by Petrén and Sjövall (1926) indicate that respiratory failure in cases of poliomyelitis can be prevented and encourage hope that recovery may follow in certain cases which would otherwise terminate fatally" [3].

A Memory of Summer Epidemics

Poliomyelitis (from Greek *polios*, gray, and *myelos*, marrow, cavity; here used as the derivative *myelon*, spinal cord), properly named acute anterior poliomyelitis and commonly spoken of as infantile paralysis, is an infectious disease caused by a ribonucleic acid virus of three distinct

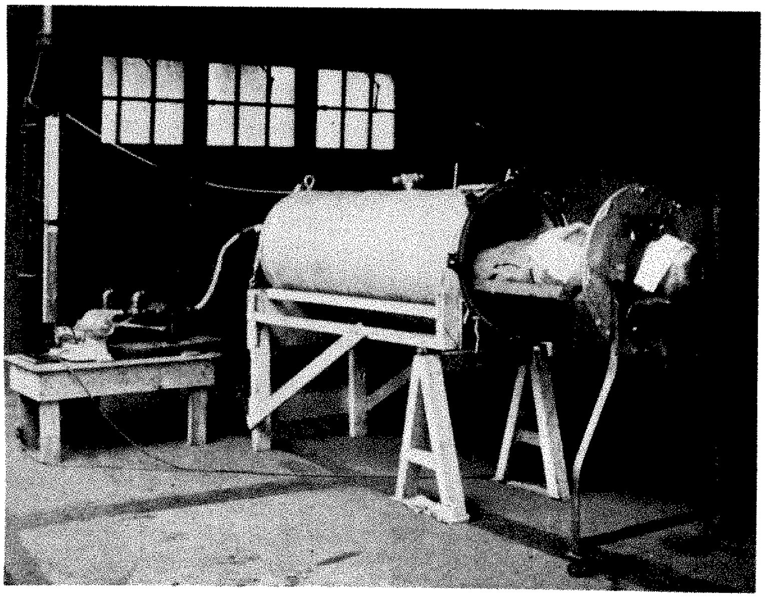

Fig 3. Tank opened at one end allowing the patient to be rolled out on casters. To do this, alternative ventilatory mechanisms had to be provided for ventilator-dependent patients. The twin electric blowers are on the low bench at left. (Reproduced from the Journal of Clinical Investigation, *1929;7:229–47, by copyright permission of the American Society for Clinical Investigation.)*

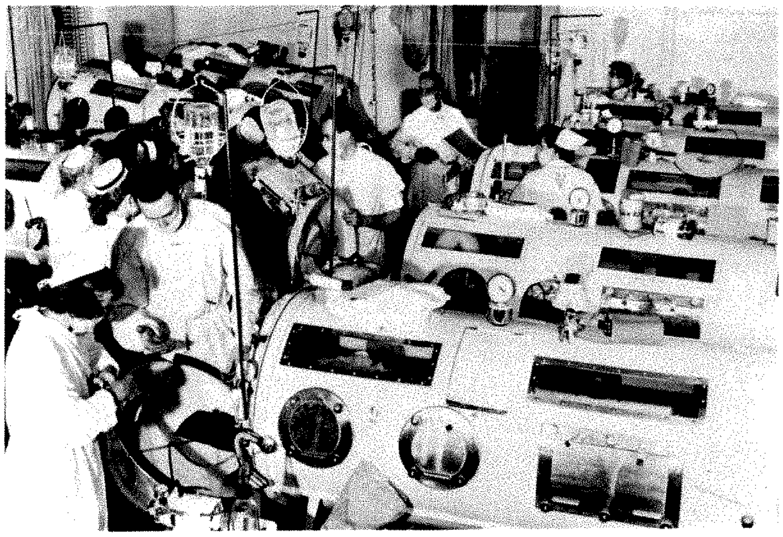

Fig 4. Respirator unit at the Haynes Memorial Hospital, Boston, August 1955. Second respirator from the front has been opened and part of the patient's body can be seen. In those days, a nurse was out of uniform unless wearing her school's distinctive cap. (Photograph courtesy of the March of Dimes Birth Defects Foundation.)

immunological types. In the days of epidemics, only a small percentage of infected persons developed clinical signs consisting of fever, headache, and stiffness of the neck and back, while fewer still developed paralysis. In a second phase of the disease, infection might localize in the gray matter of the central nervous system, with some predilection for lower motor neurons in the anterior horn tissue of the spinal cord. Only supportive treatment was possible. Of patients afflicted with paralysis, at least 50% recovered completely, whereas somewhat fewer than 25% might suffer severe permanent disability. The most serious were the cases with bulbar involvement (of the medullary centers), but respiratory paralysis could also occur without bulbar involvement by lower motor neuron damage. Respiratory failure could be managed only with a mechanical respirator.

Polio was not recognized as a public health problem in the United States until a localized outbreak occurred in Vermont in 1894. The first great summer epidemic in 1916 claimed 6,000 lives and left 27,000 others with residual paralysis. Widespread panic occurred in many cities, particularly in New York, and the tragic consequences were heightened by ignorance of the disease. The worst epidemic occurred in 1952, which left more than 57,000 people dead or paralyzed. President Franklin D. Roosevelt, himself stricken with paralysis in 1921, led the fight against polio by launching the National Foundation for Infantile Paralysis in January 1938. The National Foundation, a successor to Roosevelt's Georgia Warm Springs Foundation organized in 1927, underwrote all aspects of patient care and medical research on the disease. The Foundation's annual fund drives, synchronized with the President's birthday on January 30, took the catchy and memorable name The March of Dimes.

Treatment facilities tended to concentrate at university and city-county hospitals, each with its Respirator Center where long lines of Drinker tank respirators were lined up side by side to facilitate surveillance and care of the patients (Fig 4). The bellows of all machines, wheezing and sighing at different rates, added a surrealistic note to the scene. Patients were of all ages, including small children (Fig 5). A common rule in all respirator centers was that one professional attendant had to be present for each patient *at all times,* day and night, so that all the bellows could be worked manually in case of power failure.

A mirror held at an angle of 45 degrees over the patient's face enabled the patient to look out at the room in a normal horizontal plane, albeit in mirror image. The patient's stay might last for years. Mr Frederick B. Snite, Jr (1910–1954) of Chicago, stricken in 1936, lived for 18 years in an iron lung, but determined to live as normally as possible, he married and had three daughters during

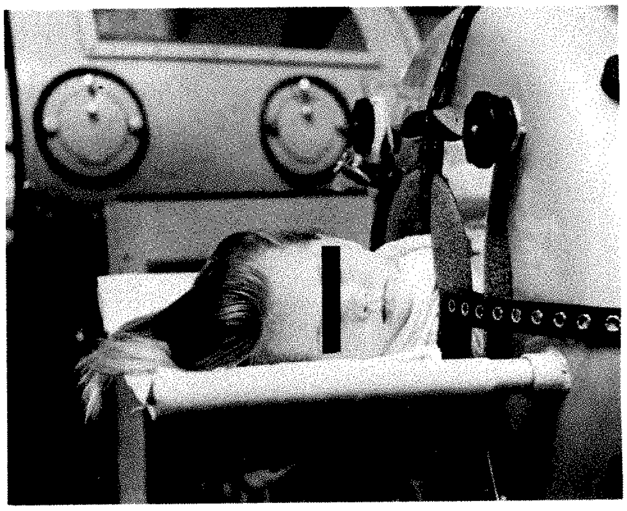

Fig 5. Child patient, aged 2 years 5 weeks, in an iron lung at the Southwestern Poliomyelitis Respiratory Center, Houston, July 1952. For small children, a moistened towel folded in one swath around the neck served to form an airtight seal without unpleasant pressure on the patient's neck. (Photograph courtesy of the March of Dimes Birth Defects Foundation.)

those years. His life was reported frequently in the newspapers and magazines, so that next to President Franklin Roosevelt, he probably was the best known victim of the disease.

Polio epidemics might seem a topic far removed from thoracic surgery, but we are in debt to Drinker and Shaw today no less than were the thousands of polio victims with respiratory paralysis.

Epilogue

Polio epidemics afflicted Western Europe as well. Lassen [5] reviewed the experience of the Blegdam Hospital, Copenhagen, in the epidemic of 1952 during which 2,722 patients were admitted. Of these, 866 showed some paralysis, 316 required special respiratory management, and 70 required artificial ventilation. The best management of respiratory paralysis was achieved by tracheostomy with placement of a cuffed endotracheal tube plus manual ventilation with a bag and 50% oxygen. Presumably, an anesthesiologist had to be with each patient at all times. Carl-Gunnar Engstrom [6] reviewed the 1949 and 1950 polio epidemics in Sweden, during which all patients with respiratory paralysis were admitted to one hospital and treated with cuirass-pattern respirators. The mortality of bulbar polio during these 2 years was about 85%; study of the cases indicated that fatality was usually due to increasing carbon dioxide retention, hence, inadequate ventilation. Engstrom designed a new mechanical respirator that incorporated active inspiration by the application of positive pressure to the airway through a tracheostomy, and active expiration by either inflation of a belt around the lower thorax or application of a negative pressure phase to the airway by a Venturi mechanism. Using this apparatus in the polio epidemic of 1953, 55 patients with bulbar polio were treated at the same hospital with a mortality rate of 27%. In this first report, Engstrom made no mention of a cuff on the tracheostomy tube.

Polio was not the sole disease requiring mechanical ventilatory assistance, even then. In 1956, Avery, Mörch, and Benson [7] described management of the crushed chest with a piston-type mechanical respirator through an uncuffed tracheostomy tube, calling their method "internal pneumatic stabilization" of the chest wall. They disposed of the idea that active expiration was necessary and found passive expiration at atmospheric pressure to be quite satisfactory. In 1957, Björk and Engstrom [8] described the routine use of a silver tracheostomy tube fitted with an inflatable rubber cuff in the management of surgical patients after major pulmonary resection. All of the foregoing machines were what we would now call volume-cycled ventilators, but the Bennett PR-1 and the Bird pressure-cycled machines were developed soon afterward.

The March of Dimes funded not only the Nobel Prize-winning research of John F. Enders, Thomas H. Weller, and Frederick C. Robbins on the growing of poliovirus in tissue culture but the work of both Jonas Salk and Albert Sabin in its entirety. In 1958, with its enemy virtually destroyed, the National Foundation for Infantile Paralysis had to choose between disbanding and finding another objective for its efforts. Such a superb volunteer organization could not be wastefully disbanded but instead changed its name to The March of Dimes Birth Defects Foundation (1275 Mamaroneck Ave, White Plains, NY 10605).

Around the country, a few Drinker respirators remain stored away in warehouses and for the most part forgotten. They are fascinating relics, reminders of the "high-tech" medicine of an earlier day.

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Intrathoracic Tumors of the Vagus Nerve

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Two patients had resection of a middle mediastinal neurilemmoma of the vagus nerve. Twenty-seven other neurogenic tumors of the intrathoracic vagus are reviewed. These tumors are generally asymptomatic except for hoarseness in an occasional patient.

(Ann Thorac Surg 1990;50:494–7)

Intrathoracic tumors of the vagus nerve are uncommon lesions occurring in the middle mediastinum. Patients are typically asymptomatic with an abnormality noted on chest roentgenogram. However, symptoms can occur from either compressive effects on surrounding mediastinal structures or recurrent laryngeal nerve involvement. Treatment consists of complete excision with preservation of the recurrent laryngeal nerve whenever possible. Two patients with intrathoracic vagal tumors are presented with a review of the literature.

Case Reports

Patient 1

A 42-year-old man with polycythemia rubra vera was noted to have a mediastinal mass on routine chest roentgenogram (Fig 1). He was asymptomatic and physical examination was unremarkable. Computed tomography of the chest confirmed the presence of a 3-cm, well-circumscribed mass in the middle mediastinum adjacent to the aortic arch (Fig 2).

Consideration was given to the diagnosis of lymphoma or bronchogenic cyst. The lack of enhancement by computed tomography with contrast infusion weighed against a lesion of vascular origin. Operation was advised and a posterolateral left thoracotomy was performed through the fourth intercostal space. When the thorax was entered, a solitary middle mediastinal tumor was readily apparent at the aortic arch anterior to the left subclavian artery, originating from the vagus nerve superior to the take-off of the recurrent laryngeal nerve. The tumor mass was firm and measured approximately 3 × 3 × 5 cm. No other intrathoracic abnormalities were noted. Complete excision was done with proximal and distal division of the vagus nerve.

The specimen was well encapsulated, weighed 10 g, and had a firm yellow-ivory color on bisection. Histologically, the tumor showed compact spindle cell formation with areas of cytoplasmic degeneration typical of Antoni A and Antoni B cells. Verocay bodies were also seen. The diagnosis of a neurilemmoma of the vagus nerve was made.

His postoperative recovery was uneventful. No change was noted in his voice, despite sacrificing his recurrent laryngeal nerve, suggesting its preoperative involvement with compensatory changes. He continues to be treated for polycythemia.

Patient 2

A 37-year-old man was seen for recent onset of hoarseness. Chest roentgenogram demonstrated a mass in the superior portion of the left mediastinum. Computed tomography confirmed the mass in the area adjacent to the aortic arch. The radiographic findings were similar to those of patient 1 (Fig 3). Physical examination was unremarkable.

Resection was advised and performed through an anterolateral thoracotomy in the fourth intercostal space. On exploration the mass was readily apparent in the middle mediastinum, extending from the vagus nerve posteriorly to the phrenic nerve anteriorly, and from the aortic arch to the apex of the chest. No other abnormalities were noted. The tumor measured 6.5 × 3 × 2 cm, was well encapsulated, and originated from the left vagus nerve superior to the recurrent laryngeal nerve. Excision was possible by enucleation of the mass. The postoperative period was uneventful, although there was paralysis of the left vocal cord as evidenced by hoarseness and substantiated by laryngoscopy.

Histologically the diagnosis of a neurilemmoma of the vagus nerve was made by the appearance of compact spindle cells interspersed with cells exhibiting vacuolar changes within their cytoplasm.

Comment

Intrathoracic neurogenic tumors are relatively common, account for 10% to 34% of all mediastinal tumors, and are generally considered to be located in the posterior mediastinum. They constitute the majority of neoplasms of the posterior mediastinum [1]. The usual site of origin is an intercostal nerve or the sympathetic chain. However, neurogenic tumors may arise from the vagus or the phrenic nerves in the middle mediastinum with tumors of the vagus being much more common than tumors of the phrenic nerve.

Tumors of the vagus are generally benign, arise from the nerve sheath, and are classified as either neurilemmoma (Schwannoma) or neurofibroma. Literature prior to 1955 often failed to distinguish between these types referring to both as neurofibroma [2]. Other terms used in the older literature were *encapsulated neurofibroma* and

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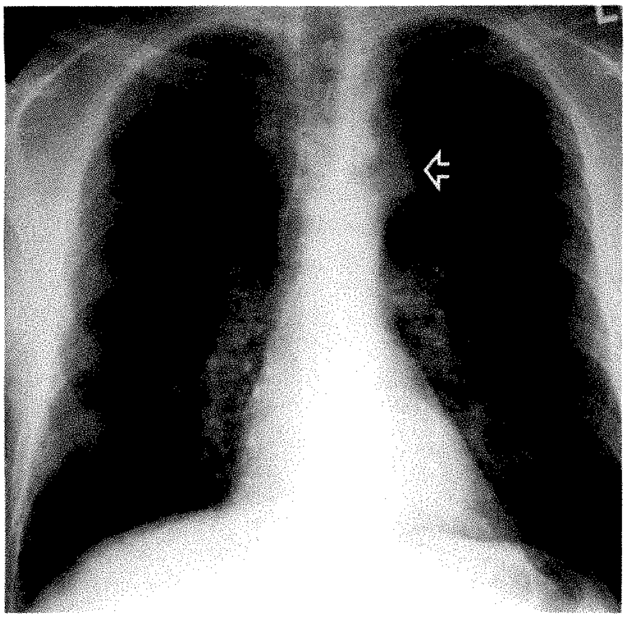

Fig 1. Chest roentgenogram demonstrating mediastinal mass.

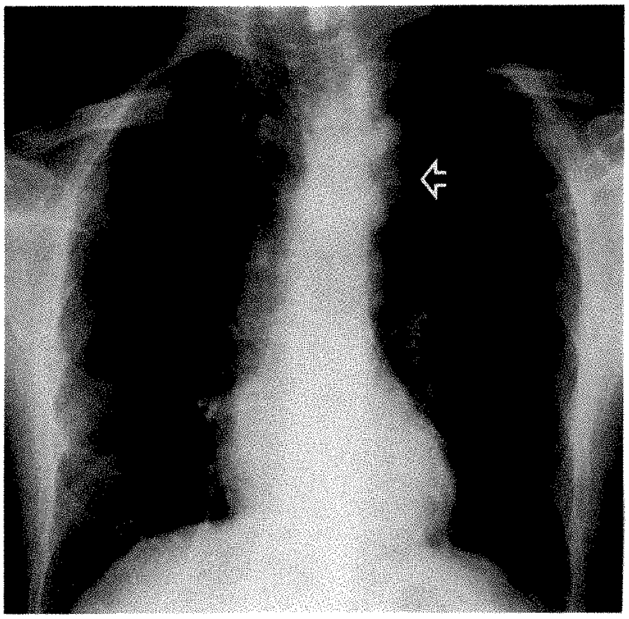

Fig 3. Chest roentgenogram of second patient with middle mediastinal mass.

perineural fibroblastoma. Malignant Schwannomas and neurofibrosarcomas of the vagus nerve have also been reported, but these are extremely rare [3].

Tumors of the vagus nerve are typically located in the middle mediastinum at the mid-thoracic level. However, neurofibromas and neurilemmomas of the vagus nerve are also found in the superior and inferior aspect of the middle mediastinum, but less frequently. Kent and associates [4] noted that the cervical portion of the vagus nerve is more frequently involved by a neurofibroma than the thoracic portion.

In 1935 Stout and Carson [5] first designated vagal tumors of nerve sheath origin as "neurilemmomas" based on the belief that they arose from Schwann cells within the sheath. Neurilemmomas are typically solitary, encapsulated, and grayish-tan in color. Histologically neurilemmomas have an organized architecture with cell proliferation occurring within the endoneurium. The cellular pattern is one of dense, avascular, palisading spindle cells that are designated Antoni type A and other cells exhibiting myxomatous changes associated with cystic areas, designated Antoni type B. The cells proliferate without invading the nerve fibers with the perineurium forming the capsule.

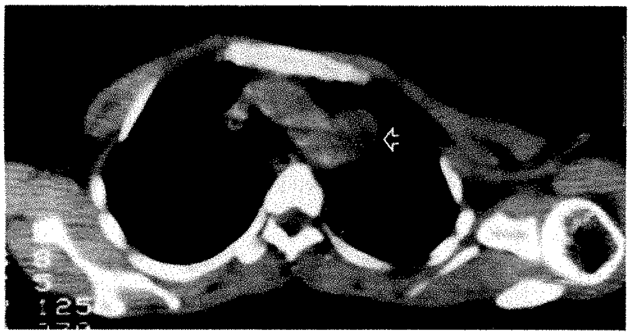

Fig 2. Computed tomography demonstrating middle mediastinal mass adjacent to aortic arch.

In contrast, neurofibromas may be multiple and are usually nonencapsulated with a disorganized proliferation of cells that invade and intertwine with nerve fibers. According to some authors, neurofibromas should be considered as hamartomas. Intrathoracic neurofibromas have an increased incidence of malignancy when associated with von Recklinghausen's disease [6].

Patients with neurogenic vagal tumors typically exhibit a paucity of symptoms and in the majority of cases are first seen with an asymptomatic mass noted on incidental chest roentgenogram. Occasionally these patients are seen with hoarseness implying tumor involvement proximal to the origin of the recurrent laryngeal nerve. Chest pain and cough may occur with tumors arising adjacent to and compressing the trachea or major bronchi.

In a review of the literature we found 27 reported cases of vagus nerve tumors [7] (Table 1). To these we add 2 personal cases for a total of 29 intrathoracic vagal tumors. Eighteen were located on the left, six were located on the right, two were bilateral, and in three instances the author did not specify. Only 2 patients had hoarseness secondary to vocal cord paralysis. Skin pigmentation suggestive of von Recklinghausen's neurofibromatosis was noted in 8 patients.

The propensity of intrathoracic vagal tumors to occur more commonly on the left side [6, 7, 23] may, in part, be explained by the fact that these tumors tend to occur in the thickest portion of the nerve where a single trunk exists proximal to the origins of major intrathoracic

Table 1. Intrathoracic Vagus Nerve Tumors

Year	Sex	Age (y)	Histology	Von Recklinghausen's Disease	Location
1943 [8]	M	35	Neurofibroma	Yes	Left multiple, below recurrent laryngeal nerve, also nerve fibers of sympathetic nerve
1950 [9, 10]	F	52	Neurinoma	No	Not specified
	M	35	Neurinoma	No	Left recurrent laryngeal nerve
	M	51	Neurofibrosarcoma	No	Right cervicothoracic
1953 [11]	M	24	Neurofibroma	Yes	Left multiple, vagus and recurrent laryngeal nerve
1953 [12]	F	60	Neurilemmoma	No	Right below recurrent laryngeal
1954 [13]	M	40	Neurofibroma	No	Bilateral above and below recurrent laryngeal nerve
1956 [14]	M	30	Neurofibroma	No	Left below recurrent laryngeal nerve
1957 [15, 16]	M	6	Neurofibroma	Yes	Left multiple, midportion
	F	39	Schwannoma	No	Left above recurrent laryngeal nerve
	F	56	Schwannoma	No	Left above recurrent laryngeal nerve
	M	30	Neurilommoma	No	Right below recurrent laryngeal nerve
	F	66	Neurofibroma	No	Left below recurrent laryngeal nerve
1959 [17]	F	67	Neurofibroma	No	Left below recurrent laryngeal nerve
1960 [18]	?	?	Neurofibroma	?	Not specified
	?	?	Neurofibroma	?	Not specified
1960 [19]	F	45	Schwannoma	No	Left recurrent laryngeal nerve
1963 [20]	M	35	Neurilemmoma	No	Left from apex to hilum involving recurrent laryngeal nerve
	M	47	Neurofibroma	Yes	Right vagus above the carina
	F	30	Neurofibroma	Yes	Left vagus below aortic arch, also tumor of 4th intercostal nerve
1964 [21]	M	17	Neurilemmoma	No	Right vagus above level of aortic arch
1965 [6]	M	35	Neurofibroma	No	Right below recurrent laryngeal nerve
1971 [22]	M	18	Neurofibroma	Yes	Bilateral; left sided tumor resected
1974 [7, 23]	F	22	Neurofibroma	Yes	Left above recurrent laryngeal nerve
	M	32	Neurofibroma	Yes	Left multiple above and below recurrent laryngeal nerve; involvement of phrenic nerve
	M	61	Neurilemmoma	No	Left above recurrent laryngeal nerve
	M	37	Neurilemmoma	No	Left above recurrent laryngeal nerve

branches. The proximal intrathoracic vagal trunk is larger on the left side, hence the tendency for these tumors to occur more commonly in this location.

When a mass is noted in the middle mediastinum on chest roentgenogram further characterization can be achieved by computed tomography. Neurogenic tumors in this location typically appear as a homogeneous, noncalcified soft tissue mass. Other considerations in the differential diagnosis should include lymphoma, bronchogenic cyst, an aneurysm of a great vessel containing intraluminal thrombus, paraganglioma, and pheochromocytoma.

We recommend exploration and surgical excision, not only to confirm the nature of the lesion, but also to prevent further growth and compression on adjacent structures. Needle aspiration of such an isolated lesion is not indicated because of the paucity of material obtained for the exact diagnosis of lymphoma and the need for resection of the other likely diagnoses.

At operation the nerve tumor in most instances can be gently dissected from the nerve after incising the epineurium. With use of a neurosurgical dissector, the encapsulated tumor, as it is generally a Schwannoma, can be separated from the adjacent nerve fibers. If it is identified as malignant by frozen microscopic examination or its infiltration into adjacent tissues, a more extensive resection is indicated. Care should be exercised when encountering bilateral lesions to prevent bilateral ablation of vagal or recurrent laryngeal nerve function.

Prognostically, recurrence of benign lesions is unusual, except in patients with neurofibromatosis, in whom additional lesions generally develop. Malignant tumors of nerve sheath origin carry a grave prognosis with patients rarely surviving beyond 1 year [1].

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Tuberculosis

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Historical

1. Koch R. The aetiology of tuberculosis (translated by Pinner B and Pinner M). Bull Int Union Tuberc 1981;56:87–100.

   This is an English translation of Dr Koch's original work on the etiology of tuberculosis read before the Physiologic Society in Berlin, March 24, 1882.

Classification, Epidemiology, and Treatment

2. Wolinsky E. Nontuberculosis mycobacteria and associated diseases. Am Rev Respir Dis 1979;119:107–59.

   This report is an extensive (592 references) review of nontuberculous mycobacterial (atypical tuberculosis) diseases.

3. Iseman MD, Sbarbaro JA. Conference on tuberculosis. Chest 1985;87:115S–49S.

   This paper reports on a conference reviewing prevention, public health issues, and treatment of M tuberculosis *and* M avium intracellularae.

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   This recent article details medical therapy for M tuberculosis *and resistant* M tuberculosis.

5. Snider DE Jr, Kelly GD, Cauthen GM, Thompson NJ, Kilburn JO. Infection and disease among contacts of tuberculosis cases with drug-resistant and drug-susceptible bacilli. Am Rev Respir Dis 1985;132:125–32.

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   This article reviews the current status of the immunological aspects of tuberculosis and atypical mycobacterial disease.

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   The abstract reports only a 56% success rate with only medical therapy in these patients.

9. Prince DS, Peterson DD, Steiner RM, et al. Infection with *Mycobacterium avium* complex in patients without predisposing conditions. N Engl J Med 1989;321:863–8.

   This paper concludes that pulmonary disease caused by M avium *can affect persons without predisposing conditions, particularly older women, and that recognition is often delayed due to its indolent nature.*

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    This report recommends a five- or six-drug antituberculosis regimen. Operation should be considered for localized disease. A 16% relapse rate is reported for patients initially successfully treated with chemotherapy.

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    This report documents the increasing drug resistance to rifampin in children.

12. Management of nontuberculous (atypical) mycobacterial infections in children and adolescents. Pediatr Infect Dis 1985;4:119–21.

    This review article covers treatment of atypical tuberculosis infections of lymph nodes, skin, bones, lung, or disseminated disease in children and adolescents.

Mycobacterial Infection and AIDS

13. Theuer CP. Tuberculosis in patients with human immunodeficiency virus infection, review of current concepts. West J Med 1989;150:700–4.

    Tuberculosis is implicated as a significant HIV-related disease. Four-drug therapy is recommended. Long-term prognosis is poor due to the underlying immunosuppression, not from tuberculosis.

14. Modileusky T, Sallter FR, Barnes PF. Mycobacterial disease in patients with human immunodeficiency virus infection. Arch Intern Med 1989;149:2201–5.

    In this study it is concluded that mycobacterial lung infection with M avium *usually occurs at or after the diagnosis of AIDS and may not cause disease.*

Surgery and Tuberculosis

15. Moran JF, Alexander LG, Staub EW, Young WG Jr, Sealy WC. Long-term results of pulmonary resection for atypical mycobacterial disease. Ann Thorac Surg 1983;35:597–604.

    Thirty-one of 37 patients having localized infection with M avium intracellularae *remained free of disease after resectional surgery. In these patients operation is recommended as the treatment of choice.*

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    This article reviews 30 thoracoplasties performed between 1970 and 1983. Twenty-three patients had tuberculosis as the underlying disease. Though a useful procedure in some, it is concluded that thoracoplasty is a rarely required procedure.

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    Between 1975 and 1984, 24 patients were operated for hemoptysis, drug resistance, possible neoplasm, or bronchiectasis. Though

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Ann Thorac Surg 1990;50:498–9 • 0003-4975/90/$3.50

the complication rate was 46%, there were no deaths and long-term results were good.

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    Twenty-nine patients underwent resection. There were two late deaths unrelated to operation. Of 27 survivors, 25 are sputum culture–negative for a mean of 36 months.

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    This article reports the complications associated with pulmonary resection, all of which can occur with operation for tuberculosis.

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    This article reports the use of extrathoracic muscle to repair or help heal intrathoracic problems, useful in the patient with resected tuberculosis.

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    Bronchopleural fistulas were successfully closed in 8 of 9 patients.

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Elsevier Science Publishing Company has recently instituted electronic publishing for certain of their journals, including *The Annals of Thoracic Surgery*. Beginning September 1st the **final version** of **accepted** manuscripts submitted on diskettes will be converted electronically directly to page proof, with a considerable saving of time and expense. Authors are encouraged to use this option if they wish to do so.

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Symposium on Thoracic Surgical Oncology

DR MARTIN F. McKNEALLY (Albany, NY): Surgical oncology has been developing as a cross-disciplinary specialty for several decades within the field of surgery. Its level of success has been variable, related in part to the enthusiasm and energy of the chief of the division of surgical oncology and the attitude of the department chairman. It also depends on the success of the research programs of the surgical oncologists, whether clinical or laboratory, and on the environment of the institution—how the oncologists and radiation therapists and others, particularly the surgeons within the department, accept the idea of a multidisciplinary program.

Some programs are very well developed. Donald Morton, Bernard Fisher, and Walter Lawrence were very active early on in the field, and they have set high standards to establish their division's position within a conventional surgical department. The cancer centers are another variation that has facilitated the growth of surgical oncology. They are analogous in our specialty to children's hospitals for the development of pediatric cardiac surgery outside the standard division of cardiothoracic surgery. Cancer centers give surgeons an undiluted exposure to multimodal therapy of cancer.

When surgical oncologists began working on a certificate of added training or special competence, thoracic surgeons became concerned about a potential problem for the training programs in thoracic surgery. The American Board of Thoracic Surgery stated that thoracic surgical oncology is a very important part of our training and that our residents must be well trained in thoracic surgical oncology. The Board suggested the thoracic surgery directors examine the state of our current activity in this area and consider what steps might be appropriate to strengthen our training in thoracic oncology. This symposium is the result of that suggestion.

I suspect that the average program is performing cancer surgery frequently enough to give a sense of "covering the subject." With a few conferences and a tumor board, graduating residents have a reasonable knowledge of the literature and the natural history and usual treatment of various thoracic malignancies. I am not convinced that their training in thoracic oncology is sufficiently thorough.

When the c-*ras* oncogene or some other abstruse word from thoracic oncology appears in the title of an article in a thoracic journal, I think the average graduate will skip over it, not for lack of interest, but because of lack of background provided within the training program. Yet, when John Minna talks about molecular genetics and biology of lung cancer at the postgraduate course luncheon, the room is packed. There is a high level of interest because we realize that this work is approaching clinical relevance, and we need to know it.

Our challenge today is to develop a rational, workable plan to enhance training in thoracic oncology. Our goal should be to match the best efforts of our colleagues in general surgery. John Niederhuber is an example, in my view, of the best in general surgical oncology. He focuses on complex resections of the liver and pancreas and runs a sophisticated laboratory studying molecular mechanisms for cancer at Johns Hopkins University. Dr Niederhuber, we appreciate your giving up a Saturday afternoon to come here and help us.

DR JOHN E. NIEDERHUBER (Baltimore, MD): Many departments of surgery have been concerned that the introduction of an organized division of surgical oncology would unfairly compete with the normal distribution of cancer cases within the department and that such a division would be disruptive to the training of residents. This latter concern has been especially acute whenever surgical oncology divisions have also sought to establish a fellowship training program. Even when departments have recruited an individual to be the "surgical oncologist," there has often been little support by the department chair for expansion of the new division into the critical intellectual mass needed. Without this critical mass, it has been difficult for these individuals to establish a clinical research and laboratory research presence in cancer surgery within the institution and nationally.

The development of this subspecialty has been further hindered by the American Board of Surgery, which has not been willing to accept the need for establishing a certification process that would serve to recognize subspecialty training in this discipline. The lack of such recognition by the American Board of Surgery has made it literally impossible for surgical oncology to establish a meaningful role for itself nationally, where it has had to compete with the strong, well-organized disciplines of medical oncology and radiation oncology. The absence of a certification process has also made it difficult to define national standards of acceptable training.

It is within the context of this experience in general surgery that cardiothoracic surgeons will need to address the question of whether a similar thoracic surgery cancer subspecialty should be encouraged to develop. Toward such deliberations, it would be useful to review the struggle of surgical oncology.

Perhaps our discussion should begin by noting the consensus conference that was organized and took place in 1981. The conference was held through the efforts of the Society of Surgical Oncology and the National Cancer Institute (NCI) with input from the American Cancer Society. The specific purpose of this consensus conference was to review the need for the creation of the subspecialty of surgical oncology and to develop training guidelines for this specialty. The conference brought together many distinguished cancer surgeons, pathologists, medical on-

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cologists, thoracic surgeons, and pediatric oncologists, as well as representatives of other disciplines—a broadly based group. The charge was to define the role of the surgical oncologist, to determine the essential elements of surgical oncology training, to define the interaction of surgical oncologists with nonsurgical specialties (such as medical oncology and radiation oncology) during the training period, and to suggest a mechanism of review and evaluation of surgical oncology training programs and their trainees. The report from this conference was published in *Cancer* in 1981 [1].

The recommendations of this panel were to establish a 2-year postresidency program of broad training in surgical oncology. The panel members felt that there should be a full-time clinical experience in radiation oncology and medical oncology during the early phase of this postresidency program. Their recommendation also stressed the need for exposure to both basic and clinical research during the training period.

In addition to the consensus conference report, Dr Steve Rosenberg wrote (in 1984) an excellent commentary regarding the issues of surgical oncology and the relationship of this subspecialty to the general surgery faculty and the Department of Surgery [2]. I would encourage you to read Dr Rosenberg's paper and would like to emphasize here that my remarks are based not only on personal experience, but also on these two published reports.

It seems clear that three factors have had considerable influence in the development of surgical oncology. First, and perhaps foremost, the development of strong subspecialties in medical oncology and radiation oncology has had a major impact on clinical surgery. The increasing numbers of medical oncologists and the role they play in the diagnosis and management of cancer patients has resulted in a declining role of the surgeon in cancer patient care. The recognition of this by surgeons has definitely been an impetus to the development of surgical oncology in an effort to restore some balance to cancer therapy.

Second, there is increasing recognition that modern cancer surgery requires a level of expertise not only in complex surgical resections, but also regarding the use of chemotherapy and irradiation. This is generally a level of expertise that is not common to every member of the general surgery faculty, and I suspect the same is also true of thoracic surgery.

Third, there is a strong desire on the part of surgery leadership to obtain a fair share of institutional and national resources allocated to cancer. These resources are substantial and, in most institutions, are largely controlled by nonsurgical disciplines.

Acknowledging that these have been the major influences behind the development of surgical oncology, let us examine for a moment the role of this subspecialty within the surgery department. As stated initially by the consensus conference, there has always been general agreement that the surgical oncologist should be expert and trained to provide consultation and care of the "difficult" cancer case. The goal is not, and never has been, that the surgical oncologist do every cancer case that comes to the department. Rather, the desire has been to have a person or persons within the department with a level of experience and training that enables them to manage the unusual cancer cases and that places them in a position to provide consultation to their colleagues in surgery and their colleagues in other medical specialties.

Their experience and training should also provide assistance to patients in selecting and sequencing different modalities of treatment. The surgical oncologist is often the patient's primary care physician, often interacting with the medical oncologists to obtain their input, arranging for consultation with the radiation oncologists, and acting for the patient as the focal point at the university to get them through the system and to obtain or provide an optimum treatment plan.

Another important role for the surgical oncologist is providing consultation to surgical colleagues and departmental leadership regarding the current status of adjuvant therapy. This leadership should extend to facilitating involvement of surgical faculty in the large national clinical trials addressing questions of adjuvant therapy.

The surgical oncologist should function as a resource for the department chair and provide leadership in establishing special clinics; for example, a breast clinic, a melanoma clinic, a sarcoma clinic. Special interdisciplinary clinics substantially improve patient care within the institution and also serve as a revenue-generating device because of their visibility in the community and their ability to attract additional referrals.

The surgical oncologist should organize and lead multimodal conferences such as tumor boards. Multimodal conferences are a very important part of patient care and are also an excellent means of resident and student teaching.

In terms of clinical research, the surgical oncologist should be able to provide the focus and organization for the department's clinical protocols in cancer. The surgical oncologist should be able to provide the integration with other oncology groups in other departments for the development and performance of these trials. In other words, by being recognized as the department's surgical oncologist, he or she will attract the interactions of the medical oncologists and the radiation oncologist as they bring their ideas forward to develop and establish new clinical trials.

The surgical oncologist also provides leadership within surgery by introducing new developments in cancer surgery to the department. The department chairman can set a priority for the surgical oncologist that will ensure that the department and its clinical programs are at the very forefront of cancer treatment.

Another important role of the surgical oncologist is to provide representation for the department on a national basis; that is, in the activities of national cooperative groups, in the activities of the American College of Surgeons Commission on Cancer, and in activities sponsored by the National Cancer Institute and the American Cancer Society.

One activity that sets the surgical oncologist and the surgical oncology division apart and establishes their program as unique and special to the department is a strong research commitment. The success of the surgical oncology program within a department can almost always be measured directly by the success of the research program. The more success the research program has, the more credibility within the department and the institution this group of individuals will have. Thus, surgical oncology can provide for the department a very important research program or research focus, valuable to resident training and to student education in surgery.

The role of surgical oncology in cancer education is important, and the division can provide assistance to the department in defining and implementing cancer education programs. This cannot be overemphasized. We tend to overlook education or relegate education to a lower priority than it deserves. The level of expertise attained by residents in the areas of cancer therapy and cancer biology at the end of their general surgery and thoracic programs often leaves a great deal to be desired. This reflects directly on our training programs, and, in many instances, adequate cancer education programs are not provided during training in general surgery.

The role of the surgeon oncologist in institutional leadership can provide the department the credibility needed to be involved in the medical school's decisions of resource allocation and policy-making as they regard the institution's cancer programs. If strength is lacking in surgical oncology, those decisions most certainly will be made on the strength of the research programs and clinical activities that are present in the other departments. From personal experience as a member of the NCI Cancer Centers Review Committee and at site visits of numerous cancer centers, I have been disappointed by the absence of an important role for surgical oncology in the leadership of these center programs.

To summarize, individuals to be trained as surgical oncologists need to have an experience, usually at the end of their general surgery training program, that will provide an opportunity to obtain the knowledge, surgical skills, and experience in management of patients with cancer, especially complicated cancer problems. In addition, they should have developed skills in cancer research. They need to develop the skills to provide leadership in cancer education and be prepared to provide institutional leadership, especially in the area of cancer. A quotation from Steve Rosenberg sums up very well the problems that exist in integrating surgical oncology into divisions and departments of general surgery. Doctor Rosenberg states, "Much energy has been devoted to 'who' should do the surgical procedure rather than to 'how' surgical oncologists can contribute to better care of patients with cancer" [2].

Where programs in surgical oncology have been successful, they have had the appropriate critical intellectual mass and have been embraced enthusiastically by the department chair. As a result, the overall clinical, research, and education programs of the department have all benefitted. Establishing a similar track in noncardiac thoracic surgery seems essential. I would like to suggest that making thoracic surgical oncology an integral part of general surgical oncology should be a consideration. There are many obvious reasons for such a coalition, intellectual and political, and such a coalition of cancer surgeons would greatly strengthen the potential of each.

DR McKNEALLY: Thoracic oncology as a field of concentration is accumulating a large body of factual material. Doctor Jack A. Roth, our next speaker, is the surgical editor of *Thoracic Oncology*, a well-written, interesting, and informative source book, which makes you realize that there is a lot more than what we teach at the bedside or in the operating room in the field of thoracic oncology. It would make an excellent fundamental text for a program in thoracic surgical oncology. Doctor Roth will discuss thoracic oncology from the unique viewpoint of a specialized cancer center, the M.D. Anderson Hospital in Houston. The thoracic surgeon in that setting is separated from most of the distractions that make it difficult for us to concentrate on education in thoracic surgical oncology.

DR JACK A. ROTH (Houston, TX): A thoracic surgical oncologist has advanced training and expertise in complex resections for thoracic cancers. At least 75% or more of the practice of a thoracic surgical oncologist is devoted to patients with thoracic cancers. A thoracic surgical oncologist has a working knowledge of multimodal cancer therapy, participates in multidisciplinary management teams, and participates in research that advances knowledge in the field.

Do we need thoracic surgical oncologists? I think there are a number of observations that indicate that such individuals with advanced training and interest in this area can play a very important role in training programs and in academic centers in the management of cancer patients.

There have been major advances in our knowledge of the biology of thoracic cancers resulting in expanding indications for surgery. For example, surgical resection may benefit patients with small cell lung cancer. Surgery is now an important component of the multidisciplinary management of esophageal cancer and pulmonary metastases.

Training remains inadequate in general thoracic surgery in many programs. I support this statement with data from the literature [3, 4]. Only 52% of training programs have dedicated thoracic surgery rotations. The thoracic case load increased in only 45% of the programs since 1982. Program directors were asked if their residency graduates could teach esophageal resection for a mid-third lesion. Only 55% answered yes. Of 126 diplomates of the American Board of Thoracic Surgery applying for recertification in 1985, only 28% indicated they performed general thoracic surgery.

In 1980, approximately 7% of major thoracic cases (7,881) were performed by noncertified surgeons. By 1985, this percentage had doubled to 14%, and because of the increasing number of cases, over 17,000 cases were now being done by non-board-certified surgeons.

The surgeon has an expanded role in the care of the cancer patient. This includes: (1) screening and early detection; (2) selection of surgical options; (3) defining the indications for palliative surgery; (4) reduction of surgical mortality, morbidity, and cost; (5) cancer rehabilitation; and (6) clinical investigations. These are expanded areas of knowledge for the cancer surgeon. It is no longer sufficient to have only technical knowledge of thoracic operations. One must have a complete understanding of the overall treatment of the patient with thoracic cancer. If we do not, we will gradually relinquish our ability to manage these patients.

Tumor biology and immunology are playing an increasing role in research and perhaps even in therapy. Cancer staging is very important and one must have a comprehensive knowledge of clinical, pathologic, and biologic staging systems.

The surgeons must be knowledgeable in assessing risks and benefits from combined modality therapy. Should we operate on the patient before chemotherapy or after chemotherapy? What is the role of radiation therapy and biologic therapy? Surgical pathology and clinical trials are also important areas of expanded knowledge.

What are the potential benefits of training programs in thoracic oncology? We can train teachers of thoracic surgery; we can train surgeons who are role models and who may attract residents to the field and train leaders for multidisciplinary groups; and finally, and very importantly, we can improve patient care.

The goal of the M.D. Anderson clinical and research fellowships is to train academic thoracic surgeons. These are individuals who can extend and improve residency training programs. They have additional training in clinical care, education, and research. This training will confer excellence but not exclusivity. The goal is specifically not to train individuals who can say, "We exclusively can operate on patients with thoracic cancer because we are specially trained in this area and others are not." The purpose of the program is to extend training and provide an added dimension to training programs in the area of thoracic oncology.

The M.D. Anderson training program provides the skills and expertise needed to manage complex thoracic oncology cases, and imparts a working knowledge of multimodal therapy. We teach skills needed to critically analyze alternatives for patient management and develop research protocols to advance knowledge in the field.

The clinical fellowship can extend from 6 months to 2 years. There is a separate laboratory research fellowship. The individual entering the research fellowship must spend a minimum of 2 years in the laboratory to obtain adequate research training. There is also an option for a third year. No clinical responsibilities are assigned during the laboratory research fellowship.

The research experience must be continuous to assure adequate time and depth. To be eligible for our fellowship one must have completed a general surgery residency program and must have acceptance in or completion of an approved cardiothoracic residency program. I feel that the residency program is the core of training for thoracic oncology. Every individual in our program must have the commitment to either complete this or to have completed the residency program prior to the fellowship.

Two options for the timing of the fellowship are available. For the first option, the individual completes the general surgery residency and then spends 24 months in research training in the laboratory for a continuous period. This is necessary for the individual to obtain the credentials to become competitive in funding and establish an independent research program. Clinical training is then done in a cardiothoracic residency program, and the individual subsequently returns for a 1- or 2-year period to obtain additional research and advanced clinical training. There may be a period when the individual joins the full-time staff as a junior faculty member.

Option 2 is somewhat less satisfactory but can result in a good experience for the trainee. The cardiothoracic residency program is completed first. There is then research training for 24 months and additional clinical training for 12 months.

The clinical Fellow participates in the overall care of the patient from initial assessment to follow-up in the clinic. The attending staff is involved in all the operations and oversees the care of the patient. Fellows actively participate in multidisciplinary conferences and journal clubs.

We also have residents who are rotating at the same time as our Fellows, and there is always some concern about competition among residents and Fellows. We have found this generally not to be the case. Our senior Fellow from 1988 to 1989 had 141 major cases, which included 74 pulmonary resections, 18 esophageal resections, and 79 bronchoscopies. The senior residents on the service, in this case from the Texas Heart Institute Program, performed a total of 207 major cases during the same time period. The general surgery residents, who come through a fourth-year level, and a second Fellow who was in the program for 6 months performed a total of 283 major cases. Thus, there is a fairly even distribution and general lack of competition for cases.

Participation in clinical research is an essential component of fellowship training. Our Fellows learn protocol design and execution and they participate in ongoing protocols, including preoperative and postoperative adjuvant therapy in lung and esophageal cancer, immunotherapy, and other studies that we have for evaluation of open lung biopsy and cardiopulmonary function tests.

Three clinical Fellows have completed our training program since 1986. Our first Fellow is an assistant professor on our staff. Our second Fellow is an assistant professor in the cardiothoracic program at the University of Cincinnati, and our third Fellow is now in his cardiothoracic residency. Although this is a small sample, I think we are beginning to realize our goal of training individuals who will participate in academic centers.

Our department is also affiliated with the cardiothoracic residency program at the Texas Heart Institute under Dr Cooley's direction. We have one resident per year who may elect a 12-month rotation at M.D. Anderson and thus also obtain additional experience in thoracic oncology.

The goal of our research fellowship is to train academic thoracic surgical oncologists who can establish new research programs in teaching institutions or upgrade existing programs. We want these individuals to be competitive for peer review funding and to develop good scientific communication skills.

We have obtained a National Institutes of Health (NIH) training grant that supports three Fellows per year in the research program. The training grant is set up so individuals may elect to go to various laboratories around the institution. At present there are 14 basic and clinical scientists who participate in the training grant, representing a number of disciplines, including tumor immunology, mechanisms of metastases, oncogenes, and mechanisms of cell differentiation.

I believe that thoracic oncology is an exciting and dynamic area, and I think we will see expansion in this area worldwide over the next 10 to 20 years. Thoracic oncologic problems represent a major challenge, and I believe this is a frontier area for research in our specialty. It is unlikely that technical refinements in thoracic surgery will produce major improvements in patient survival. However, surgical scientists, with the knowledge of cancer biology, their ability to formulate important and clinically relevant questions, and their access to tumor specimens, can assume a leadership role in thoracic oncology.

DR McKNEALLY: The surgery branch at the National Cancer Institute has a well-developed thoracic oncology program, headed by Dr Harvey I. Pass. This program has valuable lessons and resources that may be useful to thoracic program directors who are planning to train a new faculty member in thoracic surgical oncology.

DR HARVEY I. PASS (Bethesda, MD): The thoracic oncology branch at this time does not participate in any formal thoracic residency training program. We have residents, postgraduate years 2 through 5, who come to participate in a surgical oncology fellowship, and one or two of those will work with me in the laboratory. A flexible research budget is available, which is controlled by the Chief of the Department of Surgery.

The thoracic oncology section is only one part of the clinical oncology program that funds all of the intramural programs at the NCI. There are many divisions within the surgery branch and there are many divisions within the clinical oncology branch, specifically the medicine branch, pediatric branch, NCI Navy Medical Oncology Branch, radiation oncology, and clinical pharmacology branches.

In addition to its own clinical and research responsibilities, the thoracic oncology section has to take care of all the thoracic surgery and noncardiac surgery at the NIH.

Thoracic surgery at the NIH before 1980 was done by consultants from the outside; there was no formal program. The Thoracic Oncology section was established in 1981 under Jack Roth.

Doctor Roth's contributions included the systematic analysis of prognostic factors in pulmonary metastases and the first prospective, randomized trial of neoadjuvant therapy in esophageal cancers. He also did a trial comparing open lung biopsy versus empiric antibody therapy in febrile neutropenic patients with cancer. Doctor Roth's greatest research contribution was a study of tumor-associated antigens and protein products and the investigation of a monoclonal antibody that he then conjugated with ricin and used for treatment of pulmonary metastases.

At the present time the average number of cases done at the NCI in the thoracic oncology section is about 280 per year, and there are two of four possible operating days devoted to thoracic surgery. Seven of 30 beds on the surgery branch are specifically designated thoracic oncology beds, and there are two clinics per week in which we see new patients, protocol patients, and our follow-ups.

There is one thoracic oncologist at the NCI at this point, who serves as division head. There are one to two clinical research associates who spend a period of 18 months in the laboratory doing projects related to the main research theme ongoing in the laboratory. There is one full-time research assistant who assists in performing the research. There is always one clinical associate, postgraduate years 2 through 5, who is on the thoracic service to help in management of the thoracic patients, assist in the operating room, and take care of the patients after operation. They rotate every 2 months.

There is one full module devoted to bench research in the thoracic oncology section supported by about 6% of the surgery branch budget. It is divided into two parts, and is fully stocked so that you can do all the research that you want.

The research is on all levels, both in vitro and in vivo, so that the thoracic oncologist who spends time in the thoracic oncology laboratory will get three different tiers—small animal, large animal, and cellular research.

Some of the early clinical efforts involved multimodality therapy, including the use of intraoperative radiation therapy to the chest. The operating was done in a specialized operating room. There were serious complications from esophagitis. We have continued investigations in surgical excision of pulmonary metastases with a large series of patients who have sarcomas. We have also looked at histologies requiring excision of metastases, including melanoma, Ewing's sarcoma, and renal cell cancer.

Patients with truncal sarcomas and children with chest wall malignancies serve as a basis for studies of chest wall resection and reconstruction. Currently the mainstream of thoracic oncology and what we have been doing for the last 3 years is studying neoadjuvant therapy in higher-stage limited lung cancer. In a prospective, randomized trial patients who have node-positive disease are being randomized to surgery and radiation therapy versus neoadjuvant therapy.

We are also interested in exploring the use of monoclonal antibodies as an imaging agent in detecting non-small cell lung cancer; we have been studying this with the nuclear medicine department at the clinical center.

In 1986 we began to investigate the use of light-activated sensitizers for the treatment of malignancy. We have extended those investigations to the treatment of endobronchial disease. The procedure entails placing a laser fiber directly into an obstructing tumor that has been sensitized with hematoporphyrin and treating it with light. Three days later a bloodless, completely avascular tumor is removed. Photodynamic therapy is now being used with light-diffusing media to transmit the light, so that ovarian carcinoma and abdominal sarcomatosis are treatable. Within the next 6 months, we are planning to extend these studies to the chest cavity as soon as our large-animal tolerance models are finished.

Benchwork research began with animal studies for intraoperative radiation therapy and in vivo monoclonal antibody studies. The chief focus now is on in vivo/in vitro studies of photodynamic therapy for potential treatment of thoracic malignancies. We are also investigating free radical-cytokine relationships in the laboratory.

In managing a thoracic oncology program, it is important to identify one person who is able to organize clinical research protocols for the branch. That person will become the point man to whom other people will relate. This person should organize and coordinate the whole protocol, interacting with the other multimodality therapy branches. He or she must have more than passing knowledge of the benefit/risk limitations of the various treatments on an almost equal footing with the other specialties.

Where do you find such individuals? They could be home-grown, devoting an overwhelming amount of time and effort to noncardiac thoracic surgery, or could spend a 1- to 2-year surgical oncology fellowship at a major cancer institute and then come back to a thoracic oncology training program. This person must organize the teaching program for the surgical staff and the residents, as well as for students, with a curriculum that updates newer aspects of surgical oncology.

Is it not enough to have one lecture on chemotherapy and irradiation therapy and expect that that will be enough to train the residents? The only way the residents are going to learn this is for the multimodal program to be set up so that they can see it functioning in the division. That is why it is important to have a surgical oncologist who can attract and treat patients, actually delivering the chemotherapy himself or herself. This person would teach the residents what the different modalities and the different chemotherapy options are.

The thoracic oncologist in 1990 must be more than just a noncardiac thoracic surgeon. Ideally, he or she should have both clinical and benchwork experience and be able to translate this experience into ongoing investigations. The person must also be an aggressive surgeon because, although multimodality treatment is going to be the wave of the future, he or she must still be aggressive with multimodality treatment as well as in the operating room. That applies to endoscopic techniques, laser therapy, and taking care of esophageal cancer as well as lung cancer. The person must be able to collaborate with the other disciplines, incorporating these techniques into the laboratory and into the section, so that he or she will be able to use them and teach them to the residents.

Expanding biotechnology in lymphokines, growth factors, and other multimodality treatments means there should be ongoing thoracic oncologic research in a well-equipped laboratory. In setting up a laboratory for thoracic oncology, the ability to obtain and store tissue is of prime importance. I submit that this may be the most important part of a thoracic oncology research program. You have to get the tissue to do the in vitro chemosensitivity and radiation sensitivity studies, to study the oncogenes, and to study the antigens for monoclonal antibodies.

There must be different tiers of research besides the cell work. The person must be able to translate small animal work into clinical applications. The thoracic oncologist should maintain close contact with the laboratory activities, visiting daily, observing the clinical associate, guiding the technician, and performing some of the work, rather than passing everything on to a research associate. To do that, the program director will be obligated to provide protected time for this clinical researcher. If it means there must be two thoracic oncologists so that the head will be able to function independently and do his or her own research, then so be it. Protected time is crucial to get this work done.

There are several areas that I consider "hot" in thoracic oncology now that will be necessary for people to know in the next few years. Neoadjuvant therapy is already being exploited in esophageal and lung cancer, and that is the way of the future. Whether this will result in a survival benefit is not known yet. Monoclonal antibodies for early detection and imaging, as well as video fluorescein imaging, is here and is promising, especially with the early detection work from the NCI Navy. To predict how patients are going to respond to chemotherapy, in vitro chemosensitivity is being perfected. That will not be worth much until we can have pure tumor growth without any contaminating normal tissues, but the technology is promising.

Finally, newer local-mode modalities, including photodynamic therapy, may help us treat surface malignancies in the chest or pleural effusions; we are going to try to expand that at the NCI. The most exciting work is probably going to be immune modulation, the study of the molecular biology of tumors, and biologic response amplification with growth factors.

DR McKNEALLY: Nael Martini is the Chief of Thoracic Surgery at Memorial Sloan-Kettering Cancer Center, where many surgeons have come for advanced training in thoracic oncology. He has agreed to share some of his thoughts about this subject and to react to some of the things that have been said today. I particularly would like to know, Dr Martini, what you would like us as program directors to do to prepare our candidates so that they might take a faculty position with you.

DR NAEL MARTINI (New York, NY): In the past, tuberculosis is what trained thoracic surgeons in thoracic surgery. I believe that cancer trains the general thoracic surgeon of today. My focus, therefore, will be on thoracic oncology and how it should be included in the thoracic surgical training programs. For most thoracic tumors, surgery is still the primary mode of treatment. Therefore, the surgeon needs to be actively involved in decision-making in these patients. That is only possible if he or she is well versed in thoracic oncology.

There is more to cancer surgery than assessing operability or resectability. You need to know what nonsurgical disciplines have to offer either singly or in combination with surgery. We do not necessarily have to learn to give chemotherapy or irradiation but must know how and when it should be given, and what the risks and benefits are.

Many cancers originate outside the lung but have the affinity or predilection to metastasize only to lung. When is surgery appropriate on these patients? When do you recommend chemotherapy or irradiation, not because surgery is not technically feasible, but because other modalities of treatment fare better? This knowledge can only be gained by attendance and participation in tumor board conferences, and by involvement in all aspects of patient care from the moment of initial outpatient evaluation.

Thoracic surgical residents must be conversant with the natural history and pathology of all thoracic neoplasms and the treatment options available. For residents who intend to pursue an academic career, there should be an opportunity to do rotations on medical and radiation oncology services and perhaps additional time in laboratory research. At present, many thoracic surgical trainees spend most of their time in the operating room and have little or no time for involvement in special diagnostic procedures and in evaluating patients referred for surgery. They lose the opportunity to develop preoperative assessment and become involved in surgery by prescription.

There has been a progressive increase in the total number of general thoracic operations in this country, and yet a substantial percentage of noncardiac thoracic operations, up to 50% in some communities, is now performed by general surgeons, some of whom are not certified by any board. The lack of interest and availability of thoracic surgeons has created a vacuum and general surgeons have moved to fill the void. The problem is compounded by the encroachment of nonsurgical disciplines. Experience in endoscopy is lost to the pulmonary internist doing the diagnostic work-up of thoracic lesions, including performance of the bronchoscopy, and by the gastroenterologist performing the esophagoscopies, dilations, and laser treatments. In many centers, the medical oncologist dictates the course of action in treating thoracic tumors, including which patient will benefit from surgery and which will not.

Some of the operations for pleural diseases, such as for mesothelioma, or operations that involve major chest wall resection and reconstruction, or pulmonary resections of tumors invading the hilum or mediastinum can be very intricate and yet can be conducted safely. Those who perform thoracic procedures on an occasional basis may feel uncomfortable embarking on these more extensive or more intricate operations and are certainly not in a position to train others to do them safely.

Dexterity and surgical judgment are necessary attributes to any surgeon, but the knowledge that is required for appropriate case selection for treatment needs (1) case material to work with, (2) protected time to acquire the knowledge, and (3) the opportunity to mingle with other specialists treating chest problems and knowing what they can and cannot do.

The most important requirement is time. For those interested in thoracic as opposed to cardiac surgery, a 12-month concentrated training period in thoracic surgery should be offered. For those interested in cardiac surgery or combined thoracic and cardiac practice, 6 to 8 months of training in thoracic surgery should be sufficient. Lesser periods of training in general thoracic surgery are clearly insufficient. No one can master the basics of general thoracic surgery in 3 months. You need time and case material to acquaint the resident in training with endoscopy and the basic principles of pulmonary and esophageal surgery. You not only need to train the thoracic residents in the biology and natural history of all tumors, but you need to have them skillful in doing all thoracic oncologic procedures, whether they are for cure or palliation. The thoracic surgeon needs to know when adjuvant therapy is appropriate and what is available in nonsurgical options.

The case material in cancer centers is plentiful. I believe that a quarter to a third of all lung cancer we see in this country is still operable. If I were to extrapolate the numbers from that, it is 35,000 to 50,000 thoracotomies a year. If you were to distribute them to the thoracic programs we currently have, you each can benefit from 300 to 500 of these cases a year. The case material is existent if we only tap it, but this requires the availability of a dedicated thoracic surgical oncologist.

As late as 1989, a letter from Dr Orringer and the Liaison Committee on General Thoracic Surgery indicates that nearly half of the programs currently approved still have no dedicated time set aside for the thoracic residents to be trained in general thoracic surgery. Twenty-one percent of programs do not have an identifiable thoracic staff member to develop the training program in general thoracic surgery.

In our center, we currently train three thoracic Fellows a year. Although we have a recognized, approved cardiothoracic program in collaboration with New York Hospital to train thoracic residents, we have material to accommodate other programs and we already do so. For the past 3 years we have been collaborating with Bruce Reitz at Johns Hopkins in rotation; we also have on occasion rotated candidates from the Rush-Presbyterian-St. Luke's Medical Center.

Many comprehensive cancer centers have been designated and identified in this country, and I think that we ought to be able to approach them to develop similar programs.

I have confined my emphasis on the training of thoracic oncologists to pulmonary surgery simply because deficiencies in teaching esophageal surgery had already been amply addressed by Drs Pearson, Skinner, and Orringer to this group 4 years ago. I hope that this information will help us as thoracic directors, and perhaps the boards, to address and improve this aspect of training in our specialty.

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Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 16, 1992. The closing date for registration is August 1, 1991.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

CORRESPONDENCE

Certification of Perfusionists*

Invited Letter to the Editor:

The American Board of Cardiovascular Perfusion has announced that no applications for the alternative process for obtaining certification will be accepted after October 1, 1990 [1]. The alternative process permitted the consideration of individuals wishing to seek certification, but who lacked the educational requirements established by the Board. Individuals who are currently under consideration by the Credentials Committee must be able to complete verification of their equivalence in time for the 1992 examinations, after which there will be no alternative process.

Although the function of the American Board of Cardiovascular Perfusion is not related to the current real or perceived manpower shortage, this problem remains of real concern to the Board. The certification process exerts no control over the number of practitioners. Certification in cardiovascular perfusion is a voluntary activity, and there are individuals in practice who are not certified. Although the Board wishes that all practicing perfusionists would submit themselves to the preparation required for entry into the certification process, they acknowledge that this is not and probably should not be an absolute requirement for practice. The Board accepts as a basic premise that to be eligible for consideration for certification an individual must be a graduate of a perfusion education program that is accredited by an accrediting agency that is recognized by the American Board of Cardiovascular Perfusion.

Over the past 5 years more than 50 individuals have made application for consideration under the alternative process, and less than 10% have been successful in being admitted to the examination. The experience of the Board has indicated that the alternative process falls short of providing additional personnel who are fully qualified.

The Joint Review Committee on Perfusion Education and the Committee on Allied Health Education and Accreditation function as accrediting agencies of the current perfusion education programs. This year three new programs, St. Vincent Hospital and Medical Center, Portland, OR; Grossmont College, El Cajon, CA; and Quinnipiac College, Hamden, CT, were approved for initial accreditation, bringing the total number of programs to 23.

It is vital that we as the consumers of perfusionists' services encourage and promote the development of opportunities for young people to enter this field. We agree that the responsibility of the American Board of Cardiovascular Perfusion is to maintain the validity of its certificate. This can only be sustained by permitting the educational aspects to come under the review of a body outside of the Board as presently exists. We also believe that all surgeons have a duty to recruit and direct students to this important discipline.

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Reference

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*By prior agreement, this letter is being published both in *The Annals of Thoracic Surgery* and in *The Journal of Thoracic and Cardiovascular Surgery*.

Efficacy and Benefit of Mediastinal Computed Tomography

To the Editor:

We read with interest the recent article by Thermann and associates [1] on mediastinal computed tomography as a selection method for mediastinoscopy. This is an area in which we have been interested for some time and one in which we have published in the past. We feel that there are certain inconsistencies in the data presented by Thermann and associates. They have excluded 20 patients from analysis; 5 of these were excluded because mediastinoscopy was not performed despite a positive computed tomographic (CT) scan. Subsequently they included in their analysis 6 patients who did not undergo mediastinoscopy despite having CT evidence of mediastinal lymph node enlargement. This underlines the importance of analyzing all patients entered into a study.

Thermann and associates argue that as computed tomography has replaced plain tomography, the routine use of mediastinoscopy on all patients with a proven or presumptive diagnosis of operable carcinoma of the bronchus is unnecessary. We would certainly not disagree with this, and have for some time had a policy of performing preoperative mediastinal exploration only on patients with CT evidence of mediastinal lymph node enlargement, one of us (P.G.) having shown in another study [2] that in the absence of such evidence, mediastinoscopy contributes nothing to preoperative staging. In their study Thermann and associates certainly confirm that preoperative mediastinal exploration in the absence of a positive CT scan is noncontributory: they report three false-negative scans in the 63 patients subjected to thoracotomy.

However, the value of mediastinoscopy in patients with enlarged nodes on CT scanning is less clear. Thermann and associates report no cases in which the CT scan was positive and subsequent mediastinoscopy genuinely negative. The only false-positive scans were in 2 patients who fortuitously underwent thoracotomy for supposed N2 disease. From their data one could argue therefore that there is no need to confirm positive CT scans by mediastinoscopy. Goldstraw and associates [2] already showed that in 4 of 14 cases CT evidence of mediastinal lymph node enlargement transpired to be false at subsequent mediastinoscopy. Thus if we were to omit mediastinoscopy on these patients, 30% of patients with potentially curable disease would be denied thoracotomy.

In a recent study [3] we retrospectively examined 100 consecutive thoracotomies performed for non-small cell carcinoma of the bronchus in our unit, comparing preoperative staging and naked-eye perioperative findings with the ultimate histological staging. Twenty-four of the 100 transpired to have pTNM N2 disease. Only 3 of these patients came to thoracotomy without undergoing preoperative mediastinal exploration.

Both forms of staging are clearly insensitive; however, this need not be seen as a disadvantage. Pearson and associates [4] have already shown that cure after operation is possible in patients with mediastinal lymph node involvement in all but the high paratracheal nodes. It is our feeling that the patients who transpire to have N2 disease at thoracotomy despite completing the staging protocol that we employ represent a favorable subset of patients with intracapsular/microscopic deposits whose prognosis must at worst be equal to that of the patients who

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underwent "curative" resection in Pearson's study—41% survival at 5 years.

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Double-Barrel Suction Device

To the Editor:

It is the never-ending endeavor of the surgeon to keep his or her armamentarium not only effective but also as simple as possible. One of the reasons for instrumental overcrowding of the operating table is the plethora of different suction devices designed to remove blood or irrigation fluid from the operating field. The fluid removed is either discarded, processed in a cell saver unit, or, if the patient is on cardiopulmonary bypass, it may be returned into the perfusion circuit. For cardiopulmonary bypass most surgeons use a minimum of two different suction systems.

The idea occurred to me that a single suction device may be designed that is suitable to perform a "double task" by allowing the surgeon to direct shed blood or other liquids in more than one direction. Such a device (Gish Biomedical, Inc, Santa Ana, CA) was constructed of disposable plastic with a suction head with a standard tip that leads to a handle equipped with a clearly marked color-coded "thumb switch." The latter allows the suctioned fluid to be directed into a double-barrel tubing system leading in two separate directions (Fig 1). While the suction is directed in either of the two channels, the idling channel is vented through a third orifice.

This device was tested clinically and was found to be safe, simple, and cost effective compared with two separate disposable suction systems.

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Infection and Cell-Saver Use

To the Editor:

Schwieger and associates [1] found in their sample of 19 patients an incidence of Cell-Saver (CSA) bacterial contamination of 21% (95% confidence interval, 10% to 41%). They further claim that

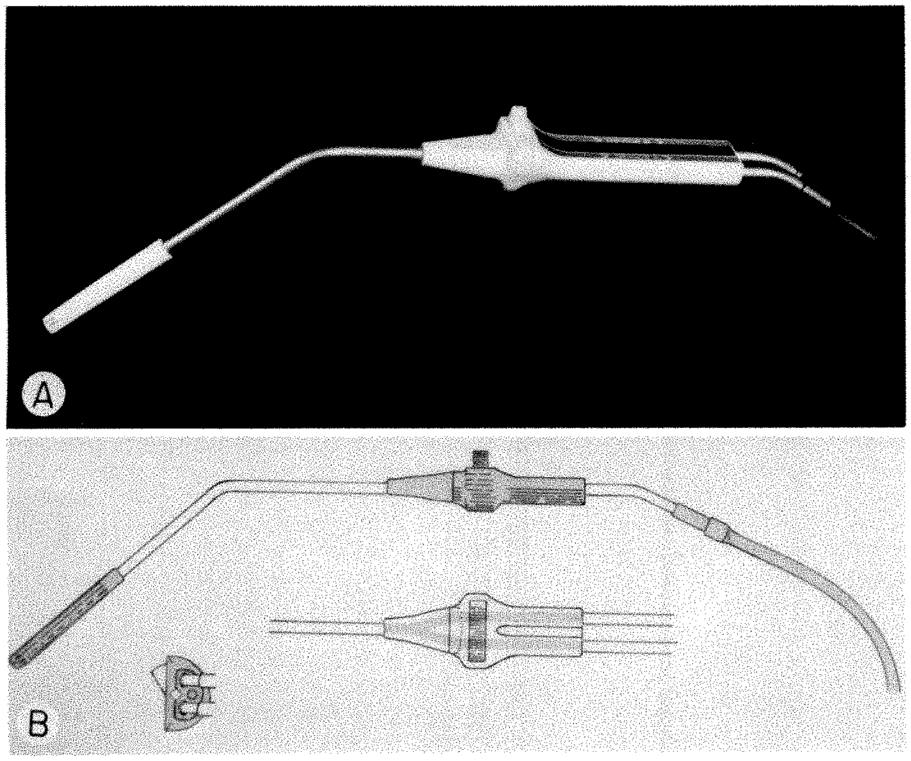

Fig 1. The "bidirectional" suction device.

patient exposure to contaminated CSA red blood cells is not "correlated" with increased risk of infection. Assuming their estimate of the risk of infection in those not exposed to CSA contamination (5/15 or 33.3%) is representative of that in the patient population in general, they would need roughly 35 subjects in each of the exposed and nonexposed groups to be able to detect (with 80% power and 95% confidence) a difference as large as a doubling in this infection rate associated with exposure to CSA red blood cells [2]. They are mistaken in accepting the null hypothesis in a very low-power study [3].

The observation of no infections among the 4 exposed patients allows one to state with 95% confidence that the maximum risk of infection after exposure to contaminated CSA spun cells is not greater than 75% [4]. Their report is also unclear as to the statistical treatment of the data. Although there is no mention of matching in the text, an unreferenced matched-pair χ^2 test is said to be the hypothesis test of choice.

Although routine use of CSA may well result in no increase in infection rate, this study provides very limited information about the true risks involved.

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Cardiopulmonary Cystosarcoma

To the Editor:

Regarding the recent article by Fleisher and associates [1], I applaud the authors' preoperative recognition of the extension of the cystosarcoma phyllodes from the right upper lobe into the left atrium. However, I would suggest that a one-stage operation that would involve the resection of the left atrial component on cardiopulmonary bypass followed by the right upper lobectomy through the median sternotomy would have certainly decreased the morbidity associated with the second operation and might have precluded the hematogenous metastasis that occurred 10 months postoperatively. It is important when doing cancer operations, even ones of this magnitude, that principles of cutting across viable tumor not be violated. I [2] have used this technique to remove a pulmonary sarcoma that was growing through the left superior pulmonary vein and entering the left atrium in a fashion similar to the case described by Fleisher and associates. During this operation, no tumor was cut across and instead a left pneumonectomy with resection of the tumor from the superior pulmonary vein with reconstruction of the left atrium was performed.

I would recommend this single-stage approach for all lung tumors that are growing through the pulmonary veins into the left atrium with the exception of tumors isolated to the left lower lobe. Control of the bronchus is difficult in these cases. However, if the pulmonary resection is done on bypass, even tumors in this location can be handled safely.

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Reply

To the Editor:

Doctor Fleisher forwarded Dr Shuman's letter to me for response as I was the surgeon primarily responsible for the care of the unfortunate lady described in "Dumbbell metastatic cystosarcoma phyllodes of the heart and lung" [1]. I agree with Dr Shuman that when therapeutically appropriate an en bloc approach is the procedure of choice for resection of malignancies. Unfortunately, medical scientific knowledge must sometimes be tempered by clinical judgment.

As outlined in the manuscript, our patient was referred for operation in a very unstable and critical condition with cachexia, recurrent life-threatening tachycardias, and congestive heart failure secondary to both adriamycin cardiomyopathy and tumor obstruction of the mitral valve. Because of the size of the tumor and its massive intracardiac extension, mobilization of the lung before bypass was considered unwise. Once the patient was on cardiopulmonary bypass and the heart opened, it was apparent that the mitral valve had to be replaced. To do an en bloc resection would have required removal in continuity of the mitral valve, the atrial tumor, the right superior pulmonary vein, and the right upper and middle lobes, followed by replacement of the mitral valve and repair of the atrium. This would have required a considerably longer procedure and cardiopulmonary bypass time than for the patient previously described by Shuman [2]. A left radical pneumonectomy with intrapericardial division of the pulmonary artery and partial excision of the left atrium in continuity, from my view of both time and technique, is not the most challenging of general thoracic surgical procedures, even though the presence of a large atrial extension requiring cardiopulmonary bypass unquestionably increases the gravity.

The decision to perform a less aesthetic cancer operation in our patient was based primarily on her poor general physical condition and the magnitude of the procedure that would have been required for en bloc resection. Additional concerns were the possibilities of coagulopathy and delayed weaning from bypass in the face of drug-related cardiotoxicity. Further, the tumor did not appear grossly or microscopically to have invaded the vein wall and it did not recur locally, as determined by follow-up echocardiograms and operation. Given the literature previously reviewed, the odds were 4:1 that other distant metastases were already present in spite of intensive patient studies that indicated otherwise. The appearance of a massive intraabdominal tumor 10 months later underlines this point. Assuming that the cardiopulmonary dumbbell and the abdominal tumors had similar doubling times, the latter would have been at least 1 or 2 cm in size (ie, 75% of the way through its life cycle) at the time of the staged cardiopulmonary procedures.

In summary, in the case reported, it was my opinion that the increased risk of operative mortality and complications with an en bloc procedure far outweighed the meager potential for benefit. I remain far more concerned about the relatively massive palliative intervention to which our patient was subjected to achieve less than 1 year's symptomatic relief and survival. However, considering the patient's age, the dire mechanically correctable circumstances when first seen, plus a small potential for long-term survival, it would be difficult to avoid intervening in similar circumstances.

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Anomalous Left Coronary Artery Surgery

To the Editor:

I read with interest the paper by Vigneswaran and associates [1] published in the October 1989 issue of *The Annals of Thoracic Surgery* concerning anomalous left coronary artery surgery, in which they propose a new method of elongating the coronary artery using pulmonary artery wall. A very similar technique was described by Dr Quentin R. Stiles 10 years ago (Fig 1) [2]. Perhaps Vigneswaran and associates would explain any differences between their technique and the technique of Stiles.

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Federal Republic of Germany

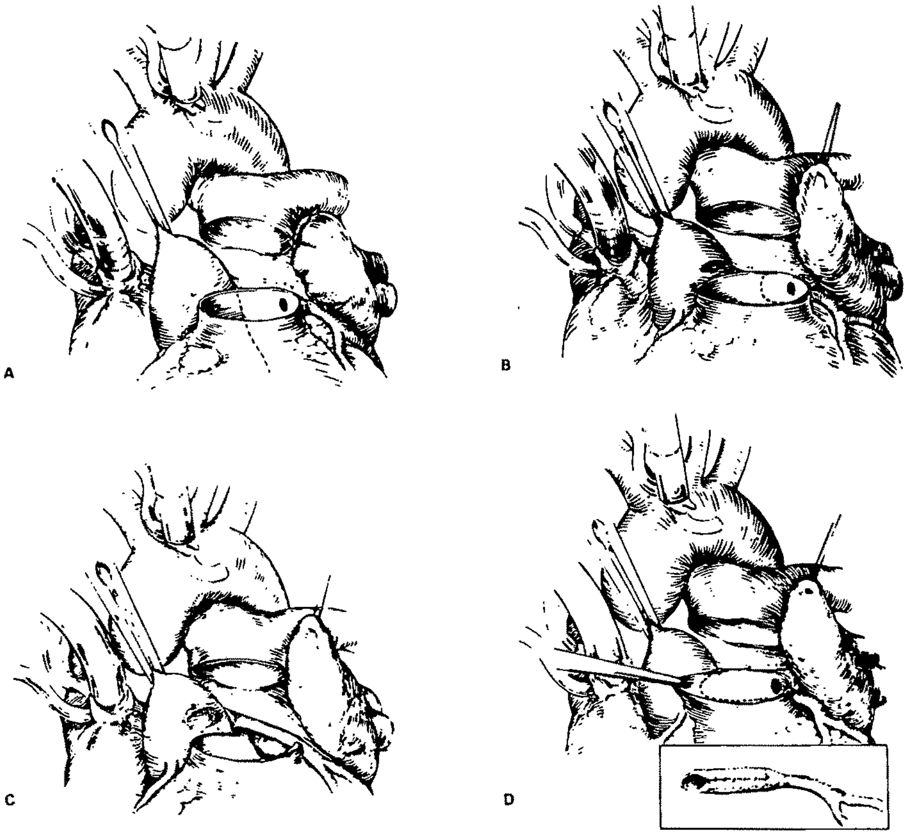

Fig. 1. Technique of transplantation of the left coronary artery from the pulmonary trunk to the ascending aorta. (A) The patient is on cardiopulmonary bypass. The aorta is cross-clamped. The pulmonary trunk is divided just above the coronary ostium. (B) The dotted line shows the cuff of pulmonary trunk to be resected. The site of anastomosis to the aorta is shaded. (C) The completed anastomosis. The divided pulmonary trunk will be reanastomosed. (D) Should extra length be needed to form a tension-free connexion, a tubular extension is fashioned from the pulmonary trunk. (Reprinted from [2] by permission of Grune & Stratton.)

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Reply

To the Editor:

Our failure to cite Dr Stiles' important work concerning extension of the anomalous left coronary artery using pulmonary artery wall was unintentional, and we wish to thank Dr Alexi-Meskhishvili for bringing it to our attention. I would like to point out two very important differences between the technique described by Stiles and that which we have recently employed. Doctor Stiles' procedure involves use of the posterior wall of the main pulmonary artery, which requires transection of the pulmonary artery and extensive reconstruction. The technique we proposed uses the anterior wall of the pulmonary artery, which allows the use of more arterial tissue and therefore a longer extension of the anomalous coronary. Furthermore, patch reconstruction technically is simple. The most important difference between the two procedures is the source of arterial blood supply to the extended anomalous coronary artery. In Dr Stiles' technique, the extension is anastomosed to the posterior ascending aorta, which necessitates aortic cross-clamping and thus produces intraoperative myocardial ischemia. In our procedure, the right subclavian artery supplies arterial blood. It is anastomosed easily to the extended anomalous coronary without aortic cross-clamping, which avoids further ischemic injury to an already compromised myocardium.

Although we appreciate the thoroughness of Dr Alexi-Meskhishvili in indicating our oversight, we feel that there are substantial differences in concept and application between Dr Stiles' technique and the one proposed in our recent article.

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Beware Centrifugal Pumps: Not a One-Way Street, but a Potentially Dangerous "Siphon"

To the Editor:

It has come to our attention once again that all man-made systems have the potential for failure. This "reacquaintance" was precipitated during two recent procedures in which an apparent malfunction of the centrifugal bypass pump allowed retrograde flow in the arterial line. This negative flow and the resultant negative pressure created a hemodynamic siphon, which, in turn, drew air into the circuit.

Unlike an occlusive roller head, a centrifugal pump is a flow-through device with wide clearances within the impeller and between the impeller and its housing. This design feature will prevent excessive outflow pressures if a line is unintentionally clamped. However, the unexpected trade-off is that there is no inherent protection against retrograde flow when the pump stops, whether because of electrical or pump failure. This retrograde flow occurs so fast that the perfusionist cannot place a clamp on the arterial line fast enough to prevent a "siphon" effect from sucking blood out of the aorta and air into the aorta from needle holes or around the pursestring suture holding the aortic cannula.

In the operating room, the sudden, mysterious appearance of air in the aortic line, when we thought we were on full cardiopulmonary bypass, caused great consternation. We all know too well the potential consequences. Our first thoughts were to check for an empty venous reservoir or ruptured tubing, but neither of these was the cause.

To purge the air, we clamped the venous and arterial lines, then transfused blood back into the venous system to maintain circulatory pressures. We then removed air from the aorta and arterial line. During this procedure it is imperative that a clamp be placed on the arterial line near the pump, otherwise opening the arterial line near the cannula to remove the air will allow the remaining blood to drain further back through the pump into the venous reservoir.

Mock circulatory studies in the laboratory show that retrograde flows can begin in as little as 540 ms after the pump is turned off. This flow can attain a value of 2.5 L/min after another 470 ms. A prototype unidirectional check valve has been constructed that prevents retrograde flow with less than 3 mL closing reflux. We recommend such a valve be used to promote safe application of centrifugal pumps.

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Membranotomy for Budd-Chiari Syndrome

To the Editor:

Chang and associates [1] were unable to explain the pathogenesis of narrowing of the inferior vena cava (IVC) after membranotomy. They suggest the narrowing was a complication of membranotomy. We have operated on 24 patients by transthoracic, retrohepatic, and retroperitoneal approach [2]. Preoperative ultrasound and venographic appearances [3] and operative findings [4] confirmed severe hourglass constriction of IVC about the level of the hepatic veins.

We prefer to label this entity as "coarctation of the IVC" [5]. The so-called membrane or septum merely completes the occlusion of the coarcted IVC similar to intimal folds completing the obstruction in coarctation of aorta [5].

Mere perforation or dilation of the membrane has resulted in reocclusion or restenosis [6]. Chang and associates report 1 such case. Longer follow-up of their patients is likely to reveal more "recurrences."

Chang and associates refer to use of only deep hypothermia to perform thrombectomy and correct the IVC stricture. This has also been done using mild hypothermia [7] and inflow occlusion techniques [8].

Both dorsal cavoatrial bypass and patch venoplasty of coarcted IVC have resulted in long-term relief of symptoms with patent grafts [8]. One of our patients had coarctation above the diaphragm that could easily be corrected by venoplasty [9].

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Intraoperative Transesophageal Echocardiography for Hypertrophic Cardiomyopathy

To the Editor:

There has been increasing interest recently in the use of transesophageal echocardiography intraoperatively to assess intracardiac features [1], which allows better visualization compared with other methods of investigation [2]. We would like to report its benefits in the operative management of 2 patients with hypertrophic obstructive cardiomyopathy (HOCM) not only in assessing the adequacy of relief of left ventricular outflow tract obstruction but also in the visualization of mitral valve structure and function.

The first patient, a 9-year-old girl with Turner's syndrome, was found to have a murmur at birth and underwent echocardiography which confirmed HOCM. Frequent severe attacks of chest pain, dyspnea, and chest infections developed throughout her childhood, despite increasing medical therapy consisting of propranolol, nifedipine, amiodarone, furosemide, and spironolactone.

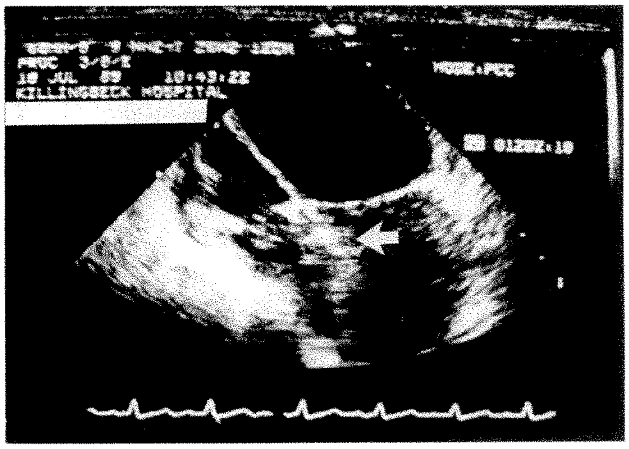

Fig 1. Transesophageal echocardiogram showing hypertrophic septum (arrow) causing left ventricular outflow tract obstruction.

She was found to have mitral incompetence and severe left ventricular outflow tract obstruction. Electrocardiogram confirmed left atrial enlargement and severe left ventricular hypertrophy. Serial echocardiograms showed grossly thickened interventricular septum with a gradient of 35 mm Hg at rest which increased to 100 mm Hg on agitation. There was grade 3/4 mitral incompetence.

Before cardiopulmonary bypass was begun, transesophageal echocardiography was performed. This showed severe mitral regurgitation with the grossly hypertrophic septum causing left ventricular outflow tract obstruction (Fig 1). After cardiopulmonary bypass was established, a left atriotomy was performed. The mitral valve chordae were short and greatly thickened with much fusion and distortion. A great deal of time was spent separating and lengthening the subvalvar apparatus. At the end of the procedure, good functional improvement of the mitral valve was observed. An oblique aortotomy was performed and the thickened interventricular septum identified. A large amount of muscle was removed, greatly enlarging the left ventricular outflow tract. The left ventricular outflow tract obstruction was removed and no residual gradient remained. This was confirmed on transesophageal echocardiography at the end of bypass, which showed marked enlargement of the left ventricular outflow tract (Fig 2) and minimal mitral regurgitation on Doppler

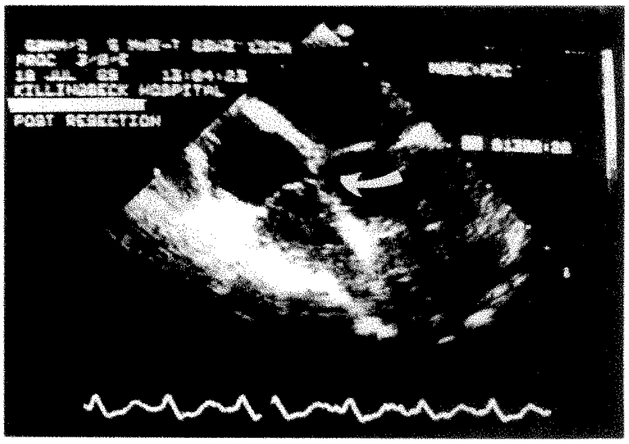

Fig 2. Transesophageal echocardiogram showing enlargement of left ventricular outflow tract (arrow) after myectomy.

studies. These were later confirmed by transthoracic echocardiography at 7 days postoperatively.

The patient made an uneventful postoperative recovery, and on follow-up 5 months later, she was very well without taking any medications and was participating actively in school activities.

The second patient, a 51-year-old woman, had increasing dyspnea associated with chest pain and palpitation over a 3-year period. She was found to have an ejection systolic murmur on examination. Her electrocardiogram showed left axis deviation and left ventricular hypertrophy. Echocardiography showed left ventricular outflow tract obstruction from HOCM with a gradient of 100 mm Hg. There was also moderate mitral regurgitation. Despite taking amiodarone, verapamil, and furosemide, she became increasingly dyspneic and was admitted acutely on two occasions with pulmonary edema.

At operation, after full cardiopulmonary bypass was established, an oblique aortotomy was performed. This confirmed thickened interventricular septum causing outflow tract obstruction. A generous myectomy was performed and the outflow tract enlarged. Transesophageal echocardiography after the patient was taken off bypass temporarily showed some residual obstruction with turbulence of flow across the left ventricular outflow tract.

Cardiopulmonary bypass was reestablished and a more extensive myectomy performed. After this, improvement in outflow tract dimension and flow characteristics was observed. Transesophageal color Doppler echocardiography also confirmed normal mitral valve function. There was no residual gradient across the left ventricular outflow tract on direct measurement.

Postoperatively the patient recovered uneventfully, with marked improvement in her exercise tolerance. Postoperative echocardiography showed no clinically significant gradient across the left ventricular outflow tract.

Histological examination of the excised specimens in both cases showed focal fiber disarray, fiber degeneration, and interstitial fibrosis typical of HOCM.

These 2 cases illustrate convincingly the benefits of intraoperative assessment using transesophageal echocardiography and Doppler flow studies in operation for HOCM. Such studies confirm the adequacy of myectomy, which is of great importance as incomplete relief of left ventricular outflow obstruction may increase the risk of early postoperative death [3]. They also allow excellent visualization of the mitral valve apparatus, confirming the improvement of mitral valve function after adequate myectomy [4], thus enabling its preservation. We believe that intraoperative transesophageal echography with color flow Doppler serves as a useful aid in the operative management of HOCM.

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CORRECTION

The article entitled "Combined coronary revascularization and splenectomy" by Ryu Koike, MD, Hisayoshi Suma, MD, Takahiko Oku, MD, Harumitsu Satoh, MD, Yoshihide Sawada, MD, and Atsuro Takeuchi, MD, published in the December 1989 issue of *The Annals of Thoracic Surgery* (Ann Thorac Surg 1989;48:853–4), contained errors in the unit notation for platelet counts.

As *The Annals* is a member-journal of the medical journal consortium agreeing to use the Systeme International (SI) units system for denoting measurements and volumes, the proper notation for the platelet count in column 1, line 10 of the text should have been $8.0 \times 10^9/L$. The same correction applies to platelet counts in column 1, the last line, and column 2, line 3.

The Annals regrets the error.

THE SOUTHERN THORACIC SURGICAL ASSOCIATION

Thirty-seventh Annual Meeting
November 8–10, 1990
The Hyatt Regency Cerromar Beach
Dorado, Puerto Rico

The Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Cerromar Beach on November 8–10, 1990, with the Postgraduate Program on Thursday, November 8, from 7:30 AM to 11:30 AM. The meeting is open to all duly qualified physicians. Both members and nonmembers are urged to register in advance.

Registration and Fees

Advance registration forms, hotel reservation cards, and details regarding transportation arrangements will be mailed to Association members. Nonmembers should write to the Secretary-Treasurer, Gordon F. Murray, MD, The Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601.

Members are not required to pay a registration fee for the Scientific Program. Residents and fellows may register without payment of a registration fee upon presentation of a letter from their chief of service. The fee for other physicians is $155, except guest speakers, authors, and co-authors. Nurses and paramedical personnel may register upon payment of a $155 fee and presentation of a letter of introduction from a member.

Registration for the Postgraduate Program is $50 for all physicians, residents, and fellows.

Presentation and Publication

Papers presented at the Scientific Session must be submitted in triplicate to the Secretary-Treasurer, Gordon F. Murray, MD, at the time of presentation, or to the Editor of *The Annals of Thoracic Surgery* prior to presentation.

Speakers for the Regular Program are limited to 10 minutes; those in the Forum are limited to 5 minutes. Speakers are asked to use the preview room prior to the opening of their session to prepare their slides for presentation.

Accreditation

The Southern Thoracic Surgical Association is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. One credit hour in category I of the Physician's Recognition Award of the American Medical Association may be claimed for each hour of participation by the individual physician.

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PROGRAM
THIRTY-SEVENTH ANNUAL MEETING
SOUTHERN THORACIC SURGICAL ASSOCIATION

November 8–10, 1990
The Hyatt Regency Cerromar Beach
Dorado, Puerto Rico

November 8, 1990 (Thursday)
Postgraduate Program

7:30 Introduction to the 1990 Postgraduate Course
Course Director, D. Glenn Pennington, St. Louis, MO

7:35 Homograft Valves and Conduits for Replacement of the Aortic Valve or Root
Ronald C. Elkins, Oklahoma City, OK

8:00 Surgical Treatment of Wolff-Parkinson-White Syndrome
Fred A. Crawford, Jr, Charleston, SC

8:25 Surgical Treatment of Gastroesophageal Reflux
John L. Sawyers, Nashville, TN

8:50 Surgical Treatment of Complex Benign Esophageal Disease
Richard B. McElvein, Birmingham, AL

9:15 Adjuvant Therapy for Esophageal Carcinoma
Jack A. Roth, Houston, TX

9:40 Break
Visit Exhibits

10:25 Surgical Treatment of Transposition of the Great Arteries
Constantine Mavroudis, Chicago, IL

10:50 Current Treatment of Coronary Artery Disease
Moderator: George C. Kaiser, St. Louis, MO

Discussants:
Morton Kern, St. Louis, MO
Joseph M. Craver, Atlanta, GA

11:30 Adjourn

November 8, 1990 (Thursday)
First Scientific Session

1:45

1. Ascending Aortic Aneurysm in the Marfan Syndrome: Results of Composite Graft Repair in 100 Patients
   Vincent L. Gott, Reed Pyeritz, Duke E. Cameron, Peter S. Greene, and Victor McKusick, Baltimore, MD
2. Determinants of Early and Late Results for Mitral Valve Replacement Combined With Coronary Artery Bypass Grafting
   Guo-Wei He, C. F. Hughes, B. D. Leckie, B. McCaughan, D. S. Thomson, and D. K. Baird, Sydney, Australia
3. Comparison of Postoperative Complication Rates in Patients Undergoing Saphenous Vein (SVG) and Internal Mammary Artery (IMA) Grafting
   Gulshan Sethi, Jack Copeland, Tom Moritz, William Henderson, Karen Zadina, Steven Goldman, and Participants of VA Cooperative Study on Use of Antiplatelet Drugs for Graft Patency, Tucson, AZ

2:30 Guest Lecturer
Cardiovascular Medicine and the Aging Population
Gottlieb C. Friesinger, Professor of Medicine, Vanderbilt University School of Medicine, Nashville, TN

3:00 Break
Visit Exhibits

3:45 **Surgical Forum**

4. Improved Lung Preservation with Cold Air Storage
   Neal D. Kon, Michael H. Hines, Charles D. Harr, A. Robert Cordell, and Stephen A. Mills, Winston-Salem, NC

5. Prolonged Pumpless Arterio-venous Perfusions for Carbon Dioxide Extraction
   Jean Deslauriers and John Awad, Ste-Foy, Quebec, Canada

6. Ischemic Spinal Cord Reperfusion Injury: The Effect of Polyethylene Glycol-Conjugated Superoxide Dismutase
   Jon M. Agee, Lorne H. Blackbourne, Terry L. Flanagan, Irving L. Kron, and Curtis G. Tribble, Charlottesville, VA

7. Severe Postischemic Injury Prevented by 15mMoles of Magnesium and Low Calcium in Crystalloid Cardioplegia
   Paul S. Brown, Jr, Fred W. Holland, Gary L. Parenteau, and Richard E. Clark, Bethesda, MD

8. Effects of Calcium Chloride Administration on the Postischemic Isolated Rat Heart
   Albert Abbott, Ronald Hill, Larry Shears, Kay Beamer, Robert Gustafson, and Gordon Murray, Morgantown, WV

9. Thyroid Function and Cardiopulmonary Bypass: "A Euthyroid Sick Syndrome"
   Fred W. Holland, Paul S. Brown, Jr, Bruce D. Weintraub, and Richard E. Clark, Bethesda, MD

10. Enhanced Pulmonary Function Using Dimethylthiourea for 12-Hour Lung Preservation
    C. Jake Lambert, Jr, Thomas M. Egan, Blair A. Keagy, Frank C. Detterbeck, and Benson R. Wilcox, Chapel Hill, NC

5:00 Adjourn

November 9, 1990 (Friday)
Second Scientific Session

8:00

11. Incidence of Late Acute Rejection of Non-Steroidal Immunosuppressive Protocol for Cardiac Transplantation
    K. Francis Lee, Janet L. Pierce, Michael L. Hess, Andrea K. Hastillo, Andrew S. Wechsler, and Albert J. Guerraty, Richmond, VA

12. The Partial Fontan Operation in Surgery for Single Ventricle
    E. Charles Douville, Robert M. Sade, and Derek A. Fyfe, Charleston, SC

13. Complete Repair of Atrioventricular Canal Malformation
    Walter H. Merrill, John W. Hammon, Jr, James R. Stewart, William H. Frist, Thomas P. Graham, and Harvey W. Bender, Jr, Nashville, TN

14. Atrioventricular Septal Repair in Infants
    Steven Bailey and Donald C. Watson, Memphis, TN

9:15 Break
Visit Exhibits

Third Scientific Session

10:00

15. Bronchoalveolar Cell Carcinoma: Factors Affecting Survival
    Richard C. Daly, Victor F. Trastek, Peter C. Pairolero, Paul A. Murtaugh, Thomas V. Colby, Ming-Shyan Huang, and W. Spencer Payne, Rochester, MN

16. Improved Survival Following Resection of Pulmonary Metastases from Malignant Melanoma
    Lyall A. Gorenstein, Joe B. Putnam, Jr, Charles A. Balch, and Jack A. Roth, Houston, TX

17. Reoperative Pulmonary Metastasectomy for Soft-Tissue Sarcoma
    Helen W. Pogrebniak, Jack Roth, Seth Steinberg, and Harvey I. Pass, Bethesda, MD

10:45 Presidential Address
Harvey W. Bender, Jr, Nashville, TN

11:30 Business Meeting (members only)

12:15 Adjourn

November 10, 1990 (Saturday)
Fourth Scientific Session

8:00 18. The Effect of Lung Contusion on Pulmonary Hemodynamics
Robert B. Wagner, Ben Slivko, Peter Jamieson, Mark Dills, and Fred H. Edwards, Rockville, MD

19. Thoracotomy in the Octogenarian
Keith S. Naunheim, Ken A. Kesler, Donald R. Judd, Stephen A. D'Orazio, Andrew Fiore, Karen Kelly, and Lawrence McBride, St. Louis, MO

20. Primary Cysts and Tumors of the Mediastinum
Amram J. Cohen, LeNardo Thompson, Fred H. Edwards, Ronald F. Bellamy, and Michael J. Barry, Washington, DC

21. Are Staples Better than Sutures for Closing Bronchi and Pulmonary Vessels?
Geoffrey M. Graeber, Joseph J. H. Collins, Jr, James L. DeShong, and Gordon F. Murray, Morgantown, WV

22. Cardiopulmonary Bypass Without Circulatory Arrest for Resection of Inferior Vena Cava Tumors with Supradiaphragmatic Extension
James R. Stewart, John A. Carey, W. Scott McDougal, Walter H. Merrill, Michael Koch, John W. Hammon, Jr, William H. Frist, and Harvey W. Bender, Jr, Nashville, TN

23. Prospective Randomized Trial of Palliative Treatment for Unresectable Squamous Cell Carcinoma of the Esophagus
Carolyn E. Reed, William H. Marsh, Leta S. Carlson, Cathy H. Seymore, and John M. Kratz, Charleston, SC

9:45 Break
Visit Exhibits

Fifth Scientific Session

10:30 24. The Internal Mammary Artery Graft at Coronary Artery Bypass Reoperation: Risks, Benefits, and Methods of Preservation
William H. Coltharp, Michael D. Decker, John W. Lee IV, Michael R. Petracek, David M. Glassford, Jr, Clarence S. Thomas, Jr George R. Burrus, William C. Alford, Jr, and William S. Stoney, Nashville, TN

25. Bilateral Internal Mammary Artery Grafts in Reoperative and Primary Coronary Bypass Surgery: A Comparative Analysis
David L. Galbut, Ernest A. Traad, Malcolm J. Dorman, Paul L. DeWitt, Parry B. Larsen, Paul A. Kurlansky, Joan M. Ally, and Thomas D. Gentsch, Miami, FL

26. Benefit From Combining Blood Conservation Measures in Cardiac Operations
James W. Jones, Robert E. Rawitscher, Thomas R. McLean, and Arthur C. Beall, Jr, Houston, TX

27. Penetrating Cardiac Injuries
Safuh Attar, John R. Hankins, and Joseph S. McLaughlin, Baltimore, MD

28. Current Indications, Risks, and Outcome Following Pericardiectomy
Patrick A. DeValeria, William A. Baumgartner, Alfred S. Casale, Peter S. Greene, Duke E. Cameron, Timothy J. Gardner, Vincent L. Gott, Levi Watkins, Jr, and Bruce A. Reitz, Baltimore, MD

29. Temporary External DDD Pacing Following Cardiac Surgery
T. Bruce Ferguson, Jr, and James L. Cox, St. Louis, MO

30. Primary Cardiac Sarcomas
Rolando Colon, Joe B. Putnam, Jr, Michael S. Sweeney, O. H. Frazier, and Denton A. Cooley, Houston, TX

12:30 Adjourn

Information About Membership in The Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) is the largest organization of its kind devoted primarily to the practice of thoracic and cardiovascular surgery. The major purpose of The Society is educational, with the aim of providing thoracic and cardiovascular surgeons from both academic and private practice environments a forum for presentation and discussion of scientific topics. As outlined in the original bylaws of The Society, this educational emphasis is designed to accomplish the broader goal of improving the quality and practice of thoracic and cardiovascular surgery as a specialty.

The STS recently celebrated its 25th Anniversary, having been founded in 1964. Since its inception, The Society has grown continually so that at present the membership includes the majority of board certified thoracic surgeons in the United States as well as thoracic and cardiovascular surgeons from 45 other countries.

In addition to an annual scientific meeting, the STS has more than 20 committees working on diverse matters related to improving thoracic and cardiovascular surgery as a specialty. Examples of these committees are: Standards and Ethics, Government Relations, Medico-Legal Affairs, Surgical Standby for PTCA, Physician Reimbursement, CPT-4 Advisory, Education and Resources, and Cardiothoracic Surgical Practice Guidelines. The Committee to Analyze Circulatory Assist Devices and Artificial Hearts sponsors topical meetings (next meeting, November 15–17, 1991, in San Francisco). The Committee to Develop a National Database for Thoracic Surgery plans to implement the first comprehensive database program for thoracic and cardiovascular surgeons in the United States; it will be offered to members in the near future.

There are five types of membership in The Society of Thoracic Surgeons: active, senior, honorary, international, and candidate.

Active Member Applicants for active membership must be surgeons whose practice is devoted primarily to the field of thoracic and cardiovascular surgery.

QUALIFICATIONS: Applicants must be Diplomates of the American Board of Thoracic Surgery or Fellows in The Royal College of Surgeons of Canada, and be established in the practice of thoracic and/or cardiovascular surgery for a minimum of three years. There must be sponsoring letters from three active STS members.

Senior Member Any active member or international member, upon reaching the age of sixty-five years, shall automatically become a Senior Member.

Honorary Member Honorary Membership shall be reserved for distinguished persons worldwide who have achieved prominence in the field of thoracic and cardiovascular surgery and have contributed to its advancement. Honorary members shall be elected by a majority vote of The Society at its annual business session upon recommendation of the Council of the STS.

International Member Members from countries other than the United States and Canada were previously accepted only as active members. Because of differences in training and practice, the application process for foreign members was often complex and time consuming. To allow for greater participation by thoracic and cardiovascular surgeons from other countries, the bylaws have been revised to provide for a category of International Member, which is the category for all members outside the United States and Canada.

QUALIFICATIONS: Applicants shall reside outside the United States and Canada. Their training in this specialty shall be considered equivalent to that of Active Members. They shall have achieved appropriate certification or recognition of achievements in this specialty in their country and must devote the majority of their professional efforts to the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee.

Candidate Member Candidate membership was created to allow participation of younger surgeons in the time prior to being qualified for active membership.

QUALIFICATIONS: Applicants shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a similar program approved for training by The Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in process of acquiring certification by the American Board of Thoracic Surgery or The Royal College of Surgeons of Canada are eligible for this type of membership.

If you would like to receive an application for membership in The Society, send the request printed below. This year's deadline for receipt of applications is September 1, 1990. We suggest you apply soon as it takes time to process the application. Approved applications will be presented to the membership at the February 1991 Annual Meeting in San Francisco.

REQUEST FOR APPLICATIONS

Please send an application for: ☐ Active membership ☐ International membership ☐ Candidate membership

TO: NAME: ____________________

ADDRESS: ____________________

____

TELEPHONE NUMBER: ____________________

Send to: James L. Cox, MD, Chairman, Membership Committee
The Society of Thoracic Surgeons, 111 East Wacker Drive, Suite 600, Chicago, IL 60601
Telephone: (312) 644-6610; FAX: (312) 938-1214

THE ANNALS OF THORACIC SURGERY
Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

Thirty-ninth Congress of the European Society for Cardiovascular Surgery, Budapest, Hungary—September 9–12, 1990

For information on this meeting, contact Budapest Convention Centre, H-1444, PO Box 233, Budapest XI, Jagello u 1-3, Hungary; or telephone (361) 852-507 (facsimile: (361) 665-636; telex: 22-7717).

Fourth Annual Meeting of the European Association for Cardio-thoracic Surgery, Naples, Italy—September 17–19, 1990

For information on this meeting, contact the Organizing Secretariat, MCM, Rione Sirignano, 5, 80121 Naples, Italy; or telephone (0)81/7611085-7611277 (facsimile: (0)81/664372; telex: 710626).

Second Annual Meeting of the International Society for Applied Cardiovascular Biology, Venice Lido, Italy—September 17–20, 1990

For information on this meeting, contact the Congress Secretariat, Kele Teo, San Marco 4930, Venice, Italy.

Interim Meeting of The Society of Thoracic Surgeons, Chicago, Illinois—September 21–23, 1990

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

Mechanical Circulatory Support 1990, London, England—September 26–28, 1990

For information on this meeting, contact Anne Sumner, Mechanical Circulatory Support 1990, Medical Research Services, 60 Oxford St, Southampton SO1 1DL, Hants, England; or telephone 0703 231068.

Controversies in Cardiovascular Disease: Surgical Versus Medical Treatment, Aalst, Belgium—September 28–29, 1990

For information on this meeting, contact Dr F. Wellens, Department of Cardiovascular Surgery, O.L. Vrouwziekenhuis, Moorselbaan 164, B-9300 Aalst, Belgium; or telephone 053/78 53 53 (facsimile: 053/78 38 76).

American College of Surgeons, San Francisco, California—October 7–12, 1990

For information on this meeting contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-sixth Annual Scientific Assembly, American College of Chest Physicians, Toronto, Ontario, Canada—October 22–26, 1990

This meeting is sponsored by the American College of Chest Physicians and the International Academy of Chest Physicians and Surgeons. For information, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association, Cerromar Beach, Puerto Rico—November 8–10, 1990

For information on this meeting, contact Gordon F. Murray, MD, Southern Thoracic Surgical Association, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610 (facsimile: (312) 938-1214).

Sixty-third Scientific Session of the American Heart Association, Dallas, Texas—November 12–15, 1990

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 750-5300.

Global Plenum on Organ Transplantation, Lucknow, India—December 14–16, 1990

For information on this meeting, contact Prof Probal Ghosh, Plenum Secretariat, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Rd, Post Box 375, Lucknow 226001, India.

Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons, San Francisco, California—February 17–20, 1991

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 111 East Wacker Dr, Chicago, IL 60601-4301; or telephone (312) 644-6610.

CLASSIFIED ADS

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Media for Medicine, Inc, 440 Park Avenue South, New York, NY 10016 (telephone: (212) 684-5540; facsimile: (212) 545-0651). All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.25 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $17.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad orders should be for a maximum of 6 months; ads may be renewed for up to 6 months at a time. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3695). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

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SITUATIONS AVAILABLE

Cardiovascular and thoracic surgeon, board eligible/certified, wanted to join well-established private practice located in Ft. Lauderdale, FL. Send CV.

Please respond to Box 251. 251L/K

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to Box 252. 252G/L

Cardiothoracic/vascular surgeon wanted to join established practice in Ohio. Recent graduate preferred. Please submit curriculum vitae and three references.

Please respond to Box 302. 302C/I

Cardiac surgeon wanted to join established private practice in Eastern PA. Primarily adult cardiac. BC/BE required. Please send CV.

Please respond to Box 315. 315D/I

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another physician in private practice in Northeast. Immediate availability. Please respond with curriculum vitae.

Please respond to Box 316. 316D/I

Excellent opportunity for recent graduate, board eligible or certified, for private practice of cardiac, thoracic, and major vascular cases in Great Lakes area. Include references and curriculum vitae.

Please respond to Box 335. 335E/J

Cardiothoracic surgeon needed for expanding program in mid-Michigan. Primarily adult cardiac and thoracic. BC/BE required. Please send CV with references.

Please respond to Box 337. 337E/J

Cardiothoracic surgeon wanted for busy, expanding Southeastern private group in regional medical center with university affiliation. Practice includes most aspects of adult and pediatric cardiac and thoracic surgery. Surgeon must be board eligible or certified with contemporary training. Excellent opportunity for suitable applicant.

Please respond to Box 342. 342F/I

Cardiovascular and thoracic surgeon: Excellent opportunity to join a busy north central Florida group. Practice specializes in adult cardiac and thoracic surgery. Excellent benefit package. Please reply with curriculum vitae.

Please respond to Box 348. 348F/K

Cardiovascular and thoracic surgeon, BE/BC, to join in 2-man private practice in cardiovascular and thoracic surgery in the Northeast. Excellent benefits package. Association will lead to partnership. Please send curriculum vitae.

Please reply to Box 350. 350F/K

Cardiothoracic surgeon needed for established program in scenic Montana. Unique opportunity for congenial private practice lifestyle combined with high-tech hospital environment including dedicated cardiac OR, cardiac anesthesia, and cardiac intensive care unit. Solo practice or association leading to partnership. Could be experienced surgeon or recent graduate from quality program.

Please respond to Box 354. 354G/L

Thoracic surgeon wanted: A busy thoracic practice 20 miles south of Boston seeks to add a third surgeon by July 1991. Candidate must be board certified or eligible. This active practice operates from a multihospital referral base. The community is an ideal area for family living, with excellent schools and nearby Boston and Cape Cod cultural and recreational facilities. Competitive salary, malpractice insurance, and excellent benefit package. Please respond with CV.

Please respond to Box 356. 356G/L

Cardiovascular and thoracic surgeon: Position available for a BC/BE surgeon to join expanding surgical practice associated with highly trained invasive cardiologists and cardiac anesthesiologists in Ocala, Florida. (Ocala is located in the center of Florida, 75 miles north of Orlando.) Excellent benefits package, including great location for family activities. Recent graduates considered.

Please send a curriculum vitae to Wayne McGraw, Executive Director, Ocala Heart Institute, PO Drawer 3130, Ocala, FL 32678. 357G/I

Cardiovascular/thoracic surgeon, BC/BE, to join well-established private practice on Florida west coast. Expertise in adult cardiac, vascular, and thoracic surgery required. Recent graduate with transplant experience preferred. Excellent compensation and benefits leading to full partnership. Please include curriculum vitae and references with response.

Please respond to Box 363. 363G/J

Cardiothoracic surgeon, BE/BC, to join established 1-man private practice involved with adult cardiac, thoracic, and vascular surgery in major Midwest community. New or recent graduate preferred. Salary leading to partnership. Please send CV, clinical experience, and references.

Please respond to Box 366. 366H/K

Vascular surgeon, board certified/board eligible, recently trained, wanted to join a busy solo vascular surgeon in north central West Virginia using 300-bed very progressive hospital. Excellent package and potential.

Please respond to Box 367. 367H/K

Cardiovascular and thoracic surgeon, board certified or board eligible, wanted for an established private practice of cardiac, thoracic, and vascular surgery in the Southeast with potential university affiliation. Initial contact should include curriculum vitae, clinical experience in all three disciplines, surgical results, and references.

Please respond to Box 368. 368H/J

Cardiac surgeon, board certified or board eligible, for very busy private practice group doing primarily adult cardiac and vascular surgery. Seeking an Associate to join well-established practice in northeast Ohio metropolitan area. Please respond with curriculum vitae and references.

Please respond to Box 370. 370H/A

Thoracic surgeon for rapidly growing group practice in the NYC area. Excellent salary. Please respond with CV and references.

Please respond to Box 372. 372H/I

Cardiothoracic and vascular surgeon, board eligible/certified with experience in adult cardiac thoracic and vascular surgery, wanted to join well-established practice located in southern California. Send CV and references.

Please respond to Box 373. 373H/I

Cardiovascular surgeon: We are looking for a recently trained B/E or B/C CV surgeon to join our very busy and enjoyable 2-man cardiovascular department at The Billings Clinic, a progressive major regional multispecialty clinic in the northern Rocky Mountain region. This is an outstanding practice opportunity for the right individual seeking a challenging and rewarding surgical practice in surroundings conducive to the highest quality of living for the surgeon and his or her family.

For further information, please call or send CV to Hewes D. Agnew, MD, or J. Scott Millikan, MD, The Billings Clinic, PO Box 35100, Billings, MT 59107-5100; (406) 256-2500. 375H/J

Thoracic surgeon, BC/BE, needed to join two others in a busy thoracic surgical practice without open heart surgery. Located in a prime suburb of NYC with a good quality of life. Rapid partnership advancement. Recent graduate preferred. Please reply with a curriculum vitae.

Please respond to Box 376. 376H/J

Cardiovascular surgeon wanted to join busy private practice in excellent Florida location. Practice includes all aspects of adult cardiovascular and thoracic surgery. Would prefer a recent graduate. Send curriculum vitae.

Please respond to Box 377. 377H/J

Cardiovascular/thoracic surgeon to complete 3-man group in adult cardiothoracic private practice in Michigan. Must be board eligible or certified. References required.

Please respond to Box 382. 382H/J

We are seeking cardiothoracic candidates for either Assistant or Associate Professor of Surgery. Applicants should have experience in surgical research and/or teaching. Applicant should be technically strong in all phases of adult cardiac surgery. Additional experience in pediatric cardiac surgery would be helpful as an extra qualification.

Please send applications to W. Randolph Chitwood, Jr, MD, Professor and Chief, Division of Cardiac Surgery, Department of Surgery, East Carolina University School of Medicine, Greenville, NC 27858-4354. Federal law requires proper documentation of identity and employability prior to final consideration for this position. East Carolina University is an equal opportunity/affirmative action employer. 383H/I

Cardiothoracic surgery group seeking an additional board eligible/board certified surgeon with interests and skills in general thoracic surgery for busy expanding practice. Private 3-man group practices in the Southeast in university-affiliated regional medical center. Practice currently includes mainly adult and pediatric cardiac and pulmonary surgery. Excellent opportunity for suitable applicant.

Please respond to Box 384. 384H/K

Cardiothoracic-vascular surgeon to join private practice—cardiac, thoracic, and vascular surgery in Northeast. New cardiac surgical program. Must be board certified or eligible. Send CV and references.

Please respond to Box 387. 387I

Cardiovascular physician's assistant—For Palm Beach County, Florida, CVT practice. Must be facile, affable, and tireless.

Send CV with references to Suite F, 11545 Old Ocean Blvd, Ocean Ridge, FL 33435. 388I

Cardiothoracic surgeon—BE/BC to join well-established CVT practice in Palm Beach County. Must be able to operate independently.

Submit CV with references to Suite F, 11545 Old Ocean Blvd, Ocean Ridge, FL 33435. 389I

Cardiothoracic surgeon (BE/BC) to join newly established practice of primarily adult cardiac surgery. Expanding practice is now ready for second surgeon. Excellent opportunity for a recent graduate in the beautiful area of Virginia.

Please respond to Box 390. 390I/J

Cardiovascular surgeon. Will perform cardiovascular diagnoses and surgery, including vein graft bypass (single, double, triple, quadruple, and higher), aortic and mitral valve replacement (single and double), vein harvest, and related surgery using traditional and laser procedures. Doctor degree in Medicine. 1 year research and clinical application of lasers to cardiac and vascular surgery. Fellow, American Board of Surgery, board eligible, Thoracic Surgery. 40+ hours per week and overtime as needed. 7:00 AM–7:00 PM. $135,000 per year. Must have proof of legal authority to work in the United States.

Apply or send resume to Job Service of Iowa, 150 Des Moines St, Des Moines, IA 50309. Job Order IA 0224378. Advertisement paid by employer. 392I

Cardiothoracic surgeon, ABTS certified/eligible, with primary interest in cardiac surgery, wanted immediately to replace member of established surgical group practicing in Allentown, PA. Competitive salary/fringe benefits. Position leads to partnership for successful candidate.

Please send curriculum vitae, clinical experience, and references to Joan M. Persa, Administrator, PO Box 8575, Allentown, PA 18105-8575; (215) 821-8790. 393I/B

Cardiovascular and thoracic surgeon: BE/BC wanted to join well-established private group practice in Philadelphia area. Seek recent or upcoming graduate. Please send curriculum vitae.

Please respond to Box 394. 394I/B

Thoracic, vascular, and general surgeon to join a busy, all boarded, private practice on eastern Long Island. Should be board certified or eligible. Excellent salary and benefits, leading to a full partnership. Send curriculum vitae.

Please respond to Box 395. 395I/L

Cardiovascular surgeon to become second surgeon in new (two year old) adult cardiac program on west coast of Florida.

Submit CV to Manatee Cardiac Surgeons, PA, 201 4th Ave East #2, Bradenton, FL 34208. 396I/K

Beautiful Hawaii: Highly regarded and successful group seeks a BC/BE cardiovascular surgeon. Excellent salary, full benefits, and superb lifestyle!

For full details contact Wendy Perlman (800) 327-1585. 397I/J

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 398. 398I/B

Chief of Cardiovascular and Thoracic Surgery: The Department of Surgery at the University of Nebraska College of Medicine is conducting a search for a Chief of the Section of Cardiovascular and Thoracic Surgery. Applications are sought from board certified individuals with interests in patient care, student and resident education, and basic or clinical research. Rank commensurate with experience.

Interested applicants should submit a curriculum vitae to Byers W. Shaw, Jr, MD, Chairman of the Search Committee, Professor and Chief of Transplant Surgery, Department of Surgery, University of Nebraska Medical Center, 600 S 42nd St, Omaha, NE 68198-3280. Applications will be accepted until a final candidate is selected. The University of Nebraska Medical Center is an affirmative action/equal opportunity employer. 399I

Cardiovascular surgeon to join a young diplomate, ABTS, in a practice that has grown to some 600 hospital surgeries per year. Location is in a city in the mid-South. The only open heart program in 15 counties. 325-bed regional medical center. 2 catherization labs. Practice consists of cardiac, thoracic, and vascular surgery. Full financial support including productivity incentive. All benefits, malpractice and office expenses provided.

Please respond to Box 400. 400I

Pennsylvania CT group practice—The Geisinger Medical Center & Clinic seeks CT surgeon with transplant experience to join existing group of 7 (3 CT/2 vascular/1 intensivist/1 consultant plus 9 PAs). The Clinic has 460+ attendings/195+ residents with service area of 2MM+. The department handles 1,400+ cases (530+ opens); has 90% internal referrals. Family area, good schools, 3 hours to NY/DC/Philadelphia, excellent comp package.

Call/send CV to Carole Gregory, c/o MedQuest, PO Box MQ, Devault, PA 19432; (215) 640-3774. 401I

Develop OH Program—Geisinger Medical Center & Clinic in Pennsylvania seeks CT surgeon for new OH program at affiliated community hospital. Projections include 130 OH cases in first year, 250 in second. All professional/technical support and coverage provided plus full compensation package.

Call/send CV to Carole Gregory, c/o MEDQUEST, PO Box MQ, Devault, PA 19432; (215) 640-3774. 402I

Cardiovascular and thoracic surgeon: Excellent opportunity for a board certified/eligible cardiovascular and thoracic surgeon to join in a new, growing department in a metropolitan New York community on Long Island. Academic/private practice setting with excellent compensation. 533-bed community teaching hospital. Experience in electrophysiologic surgery, artificial devices, and/or transplantation helpful. Please respond with curriculum vitae.

Please respond to Box 403. 403I/L

SITUATIONS WANTED

Cardiothoracic surgeon, 36, 2 years' experience in adult cardiac surgery. Excellent results. Wishes to relocate to West Coast or the Northwest.

Please respond to Box 369. 369H/J

Thoracic and cardiovascular surgeon, board certified, with broad experience in all phases of the specialty except transplantation wishes to relocate. Curriculum vitae and references on request.

Please respond to Box 371. 371H/I

Cardiovascular and thoracic surgeon, 45, ABS, ABTS, NE university trained, seeks relocation. Experienced, publications, academic appointment.

Please respond to Box 386. 386I/K

Cardiovascular and thoracic surgeon, 52, looking for a salaried position in cardiac surgery or serving as assistant surgeon. ABS, ABTS certified. Experienced in every facet of the field. May start immediately

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Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street Suite 312, Sacramento, CA 95819. 364G/L

Clinical cardiac surgical fellowship at Massachusetts General Hospital, Boston, Massachusetts: One-year appointment beginning January 1, 1991, or July 1, 1991. Salary commensurate with training and consistent with hospital scale. Intensive exposure and experience opportunity in cardiac surgery. PG-5 or beyond. Interviews and references required.

For additional information, please write Mortimer J. Buckley, MD, Chief, Cardiac Surgery, Massachusetts General Hospital, Boston, MA 02114. 385I/J

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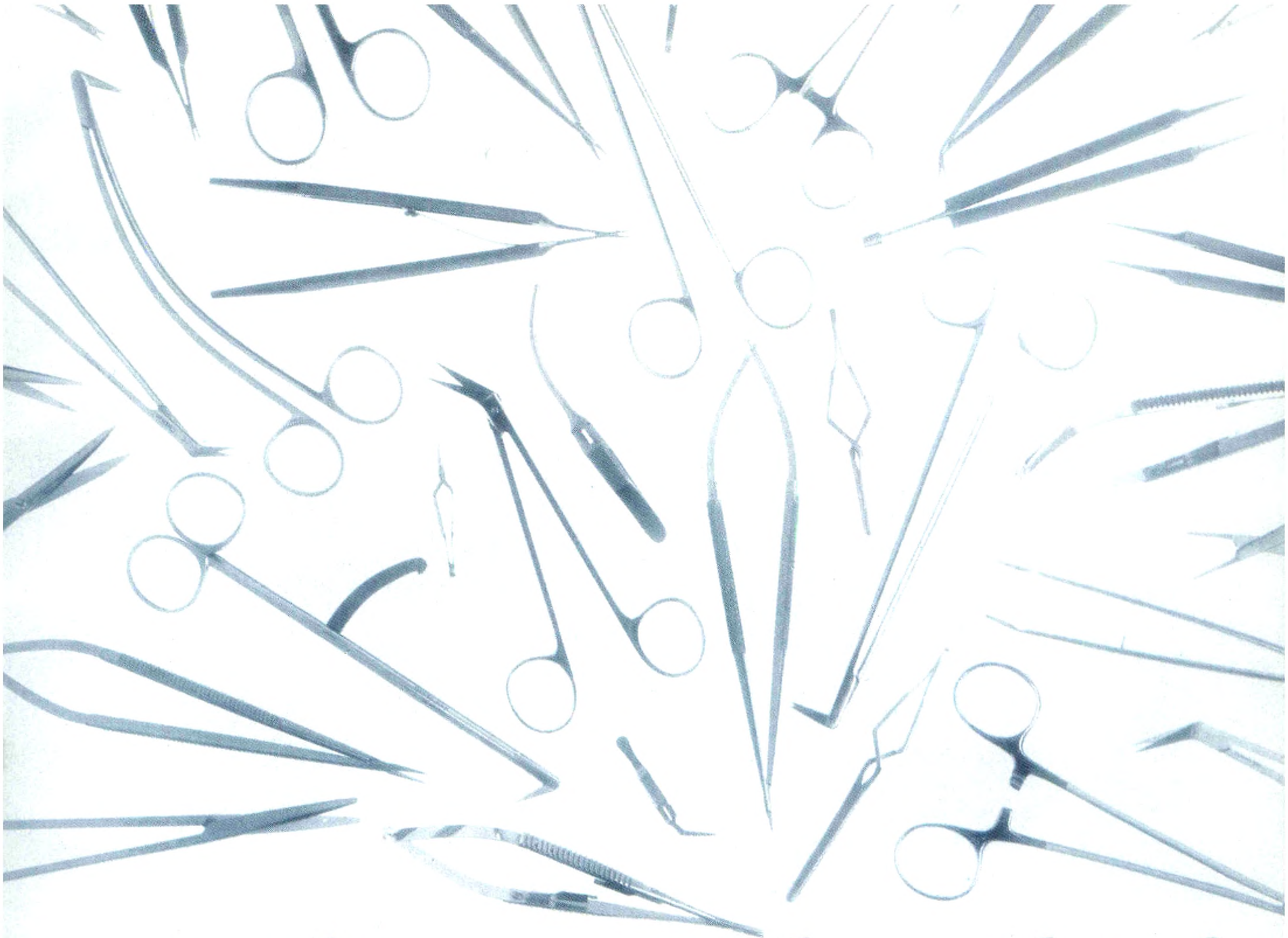

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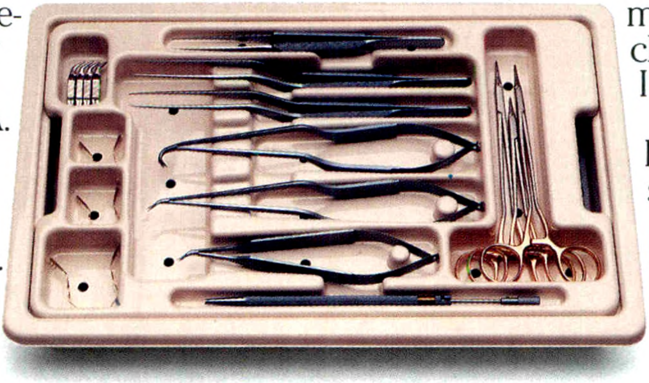

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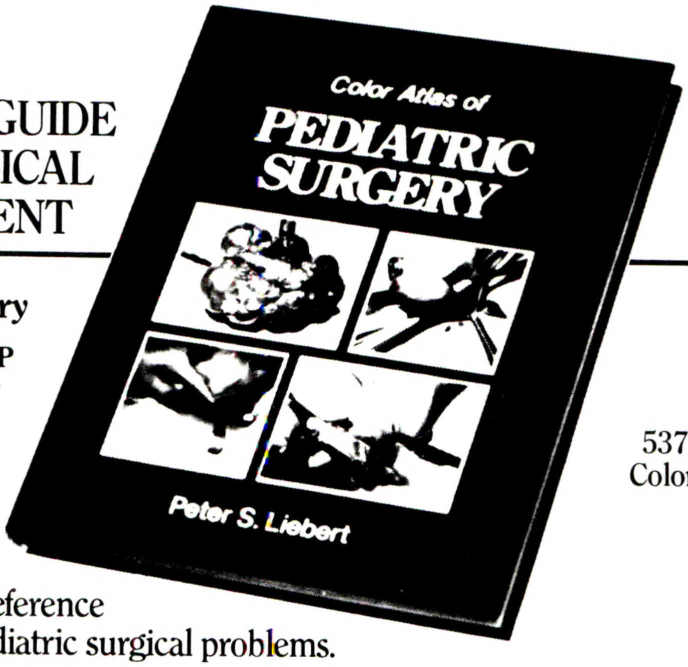

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1. Pairolero PC, Arnold PG. Chest wall tumors: experience with 100 consecutive patients. Journal of Thoracic and Cardiovascular Surgery 90:367-372, 1985.
2. Brown GL, et al. Comparison of prosthetic materials for abdominal wall reconstruction in the presence of contamination and infection. Annals of Surgery 201(6):705-711, 1985.

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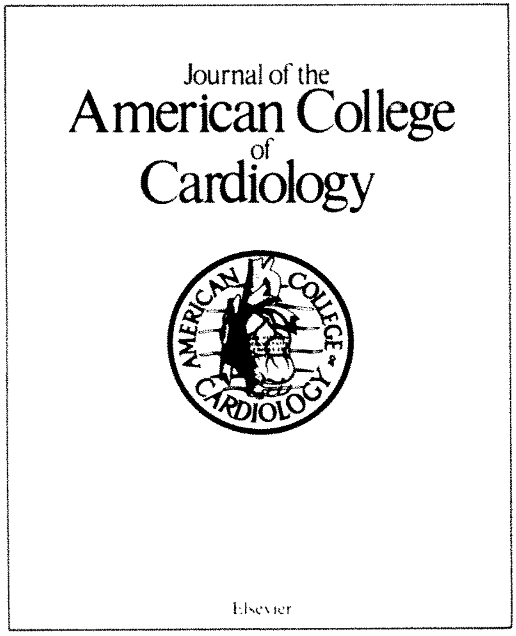

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Pulmonary circulation - advances and controversies

edited by **C.A. Wagenvoort** *and* **H. Denolin**

The Working Group of Pulmonary Hypertension of the International Society and Federation of Cardiology was formed in Prague in 1984. It was decided then to include in its aims the preparation of reviews and comments and the identification of controversies regarding the pulmonary circulation and pulmonary hypertension in particular. Implementation of this commitment, however, appeared quite difficult and it was decided that the task of the Working Group should be realized in the form of a book.

This book focuses on a number of topics within the field of the pulmonary circulation in which there have been recent advances or important developments, or in which controversial issues are at stake.

It will no doubt serve not only as an up-to-date source of information but also as a stimulus for further research to cardiothoracic surgeons, paediatricians, anaesthesiologists, intensive care physicians and pathologists, as well as cardiologists and pulmonologists.

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